JPRS-EST-86-017

15 AUGUST 1986

Europe Report

SCIENCE AND TECHNOLOGY

FBIS FOREIGN BROADCAST INFORMATION SERVICE

NOTE

JPRS publications contain information primarily from foreign newspapers, periodicals and books, but also from news agency transmissions and broadcasts. Materials from foreign-language sources are translated; those from English-language sources are transcribed or reprinted, with the original phrasing and other characteristics retained.

Headlines, editorial reports, and material enclosed in brackets [] are supplied by JPRS. Processing indicators such as [Text] or [Excerpt] in the first line of each item, or following the last line of a brief, indicate how the original information was processed. Where no processing indicator is given, the information was summarized or extracted.

Unfamiliar names rendered phonetically or transliterated are enclosed in parentheses. Words or names preceded by a question mark and enclosed in parentheses were not clear in the original but have been supplied as appropriate in context. Other unattributed parenthetical notes within the body of an item originate with the source. Times within items are as given by source.

The contents of this publication in no way represent the policies, views or attitudes of the U.S. Government.

PROCUREMENT OF PUBLICATIONS

JPRS publications may be ordered from the National Technical Information Service, Springfield, Virginia 22161. In ordering, it is recommended that the JPRS number, title, date and author, if applicable, of publication be cited.

Current JPRS publications are announced in Government Reports Announcements issued semi-monthly by the National Technical Information Service, and are listed in the Monthly Catalog of U.S. Government Publications issued by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

Correspondence pertaining to matters other than procurement may be addressed to Joint Publications Research Service, 1000 North Glebe Road, Arlington, Virginia 22201.

JPRS-EST-86-017

15 AUGUST 1986

EUROPE REPORT

SCIENCE AND TECHNOLOGY

WEST EUROPE

EAST EUROPE

CHEMICALS/PHARMACEUTICALS

FACTORY AUTOMATION

SCIENTIFIC AND INDUSTRIAL POLICY

/9987

WEST EUROPE/AEROSPACE

SELENIA TO HEAD SATELLITE RADAR R&D FOR ESPRIT

Milan SISTEMI E AUTOMAZIONE in Italian Apr 86 p 356

[Text] Within the scope of ESPRIT, the strategic program of research and development in data processing technologies, the EEC Commission has awarded to a group of European firms and research agencies, headed by SELENIA (IRI-STET Group), a contract for a design study on a new generation of systems capable of using satellite radar readings in real time.

The Group is made up of Dornier (FRG); GEC Research and Hunting Technical Services (Great Britain); Thomson CSF (France); the Polytechnic Institutes of London and Milan; and the ESIEE, the Higher School of Engineering in Paris.

Radar readings are the only usable ones in all-weather conditions, but the processing of the data provided by the present system requires several hours. In March of last year, this group of firms had submitted to the EEC authorities a 5-year plan for the development of new image-processing technologies, proposing the design and building of a satellite radar system that could be used, in particular, for the monitoring of farm crops, surveillance of the seas for maritime safety, and pollution control.

The EEC has now approved the program insofar as concerns the feasibility and definitional studies of the system, and will underwrite 50 percent of the costs. The project, which has been designated ARTSIP [Adaptive Real Time Strategy for Image Processing] has also attracted the keen interest of the ESA [European Space Agency], which is evaluating it for possible integration into its own programs.

9399
CSO: 3698/473

ACHIEVEMENTS OF EEC'S BIOMOLECULAR ENGINEERING PROGRAM

Paris BIOFUTUR in French May, June 86

[Article by E. Magnien*: "Genetic Engineering for Agriculture"; first four paragraphs are introduction]

[May 86 pp 55-59]

[Text] Started in 1982, the genetic engineering activities of the Biomolecular Engineering Community Program (BEP) on agriculturally significant species reached their conclusion on 31 March 1986. The contractors' final meeting, which was held at Wageningen on 27-30 January 1986, has been used as a basis for the preparation of a scientific evaluation report that is reflected in this article, the second part of which will be published in June.

It should not be assumed that all the results described in this article are to be exclusively credited to the community program. Many of the research programs mentioned here would also have a high priority within national programs, in the absence of a European framework. Furthermore, since these are contract activities sharing expenses, the EEC Commission cannot claim more than 50 percent of the research funds invested in these activities that it finances jointly with national institutions or, as the case may be, private companies. In any event, the budgets involved are small since they allow the financing of only one or two researchers per laboratory. But that is not the question. What is important is to know whether sharing these scattered resources, within an international framework, is likely to have a more-than-additive impact on the technological progress that results from it. The answer is certainly positive: Indeed, the BEP program never stopped mixing scientific ideas conveyed from one point of the continent to another, bringing together fragmentary skills, uniting physical force and gray matter against major methodological obstacles, promoting the mobility of the youngest researchers to help their interdiscipline training and, needless to say, their multiculture experience. The momentum given by the community program can be first compared to a catalytic effect. The coordination established between the contracting laboratories, in whatever form it assumed, meetings, visits, contractors' joint efforts, collective publishing, has been primarily aimed at upsetting conformities

* Biotechnology and Genetics Division (DG XII/F/2), EEC Commission.

that could have lured established scientific thinking.* Community financing means funds invested for thinking and achieving **TOGETHER AND DIFFERENTLY.**

From this, a new type of centers of excellence may emerge, i.e., not the gigantic laboratories that some organizations could certainly dream up or even build, but large "institutes without walls" made up of a variable number of laboratories, encompassing numerous fields of expertise in several different member states, connected merely by the organic links of the European program.

What could be construed as a figment of the imagination has actually taken shape in five specific areas of a large sector of the Biomolecular Engineering Program: genetic engineering of agriculturally significant species. The question that executives of this community project, in the Commission or within the national delegations, would like to be able to answer is how to know if, after approximately 3 years of joint research, these "institutes without walls" are really beginning to come into existence in the fields of molecular biology of symbiotic interactions; genes and vectors derived from Ti [tumor inducing] and Ri [root inducing] plasmids; plant nuclear genes; plant cytoplasmic genes; protoplasts and their manipulations.

Symbiotic Genes

The main effort was devoted to molecular genetics of nitrogen-fixing symbiosis between leguminous plants and Rhizobium (nine laboratories involved) and spilled into exploratory studies of other interactions beneficial to plant productivity (two laboratories involved).

1. Nitrogen-Fixing Symbiosis With Rhizobium

The contractors devoted their analysis to three genetic components of the system: bacterial genes controlling the early stages in the achievement of symbiosis, bacterial genes active during the terminal differentiation phase of nodules and involved in nitrogen-fixation metabolism, and finally, the plant partner's genes that keep up a permanent "dialogue" with the harbored microsymbiote:

-- The initial phase in the achievement of symbiosis is beginning to reveal its secrets, thanks to the identification of at least eight nod [noduline] genes, all sequenced, some of which (nod ABC) appear highly conserved from one Rhizobium species to another, whereas others have a higher degree of specificity in keeping with the characteristic host range of the species. In particular, there are some that exert a positive control over the association with a homologous host ("Tom" genes of a Rhizobium leguminosarum strain originating from Central Asia); others exert a negative control that removes the possibility of any association with a heterologous host. Some of these genes have been attributed a function based on sequence data and, as the case may be, on isolation of the product. Several nod genes should code for membrane proteins (nod ABCIJ); nod F specifies a protein involved in acetylation reactions. Nod D is a regulator gene controlling the whole system and subordinated to a light-molecular-weight substance present in the **root** exudates

* The list of contractors is available. Contact the author: Biotechnology and Genetics Division (DG XII/F/2), EEC Commission.

of peas or broad beans. These function studies, which will have to be continued, will make it necessary to have closer collaborations between molecular biologists and biochemists;

- The metabolism of the nitrogen-fixing nodule remains the most obscure part of the symbiotic system. In several Rhizobium species, nif [nitrogen-fixation] genes homologous to known equivalent genes in Klebsiella pneumoniae have been identified. Other genes necessary to nitrogen fixation (fix), whose function, however, is not known, have been found in R. meliloti. As in most of the rapidly growing Rhizobia, these genes are carried on the symbiotic plasmid pSym, in which they are usually found grouped, in the vicinity of nod genes, within a region of a few dozen kilobases. But two contractors have shown a greater dispersion of nitrogen-fixation genetic controls, with the discovery of a fix region 200 kb [kilobases] away from the main nif-fix/nod region, and the detection of genes, carried on a different plasmid, that are capable of modulating the nitrogen-fixing ability of the strain. It appears that advanced studies of nodule physiology, taking advantage of the molecular tools that are now available, are definitely needed. One of the contractors has also paved the way in this area. By modulating the level of cyclic AMP [adenosine monophosphate] of a strain in which the adenyl cyclase gene has been manipulated, or by constructing transposition mutants that are deficient in succinate transport, he succeeded in showing the role played in nitrogen fixation by genes that govern carbohydrate metabolism, especially at the level of the Krebs cycle and of energy supplying;

- The plant partner's genes are beginning to be better known. A method for isolating absorbent hairs without root contamination allowed to detect the existence of proteins specific to these cells, that are the first ones to be recognized by Rhizobium. Some proteins are soluble, others are associated to the membrane. Other contractors undertook to find genes for nodulines, proteins of the host plant specific to the nodule, of which there are approximately 10 in the species under consideration.

Several noduline genes have been cloned and the coordination of their expression during nodule development will have to be clarified shortly. The coordinated expression of leghemoglobin genes (protecting bacterial nitrogenase against ambient oxygen) in this development program has already been described with precision. As mentioned elsewhere, the leghemoglobin gene promoter has functioned, under the required conditions of tissue specificity, after transfer to a heterologous host: This is a useful expression system for a more precise study of the sequences that are responsible for the coordinated activation of this family of genes specific to the nodule. Mutagenesis of the plant partner should complete these studies, in order to identify other genes whose product would not accumulate in the nodules, which would be the case, in particular, of regulator genes.

2. Studies of Other Beneficial Interactions

It has now been demonstrated, thanks to the work done in a contractor's laboratory, that siderophore-producing strains of Pseudomonas putida are capable of increasing potato crop yields by competing with harmful microorganisms in the soil.

The role of siderophores, particularly in their effect on iron absorption by the plant, is not clear, however. The system is nevertheless sufficiently promising, and the genetic manipulation prospects of Pseudomonas are interesting enough, for this line of research to be further explored. The main question, which has not been tackled yet, is the interaction of the strain with the plant, and the possibility of making it genetically subservient, in other words, its competitiveness in the soil would be dependent on the presence of the cultivated species.

Another group did some exploratory work on ectomycorhyzae whose fundamental role in the nutrition and health of woody plants is well known. There are very few studies of these fungi from a molecular point of view; everything still remains to be undertaken, but preliminary results are confirming researchers in their hope of genetically manipulating some useful species. In Morchella conica, linear plasmids have been isolated, they are being analyzed for the possible existence of a point of origin for replication. Nuclear DNA sequences and mitochondrial DNA sequencies have also been cloned. This approach constitutes a preliminary step to any subsequent manipulation, particularly for the purpose of being able to construct vectors.

Considered as a whole, the field of symbioses is counted among the most active in the program, with four patents taken and a number of collaborations that corresponds to more than 2.3 times the number of laboratories involved (see figure 1). In this way, a web of international relations for the study of plant-microorganism relations is being formed in Europe; it is still thin in actual size, but through it shines a dynamism that augurs well.

Agrobacterium Ti and Ri Plasmids

The bacteria Agrobacterium tumefaciens and Agrobacterium rhizogenes have been carried to the heights of fame, it is now a well-known fact, by their natural ability to "micro-inject" foreign DNA into the chromosomes of infected plant cells. The genetic transformation of the host plant is manifested by the appearance of tumors or of hairy roots, depending on the case; this occurrence is the result of the expression of oncogenes that have been transposed from bacterial plasmids (Ti or Ri plasmid) into the plant genome where they are expressed constitutively. Even before they were able to discover all the steps that govern the infection process of wounded tissues and the transfer of bacterial T-DNA [transferred DNA], several teams quickly succeeded in taking advantage of this natural transfer system and in subverting its original purpose to turn it into a genetic engineering tool.

The extent of applications of such a system, both for long-term varietal creation and for deeper genetics and physiology studies at the molecular level, is deemed so great that the number of laboratories striving to assimilate Ti or Ri plasmid technology is constantly increasing.

During the first meeting of the Biomolecular Engineering Program at Louvain-la-Neuve in November 1983, R.B. Flavell (PBI [Plant Breeding Institute], Cambridge) set it as a strategic objective that the contracting laboratories involved in plant molecular biology should succeed in mastering this

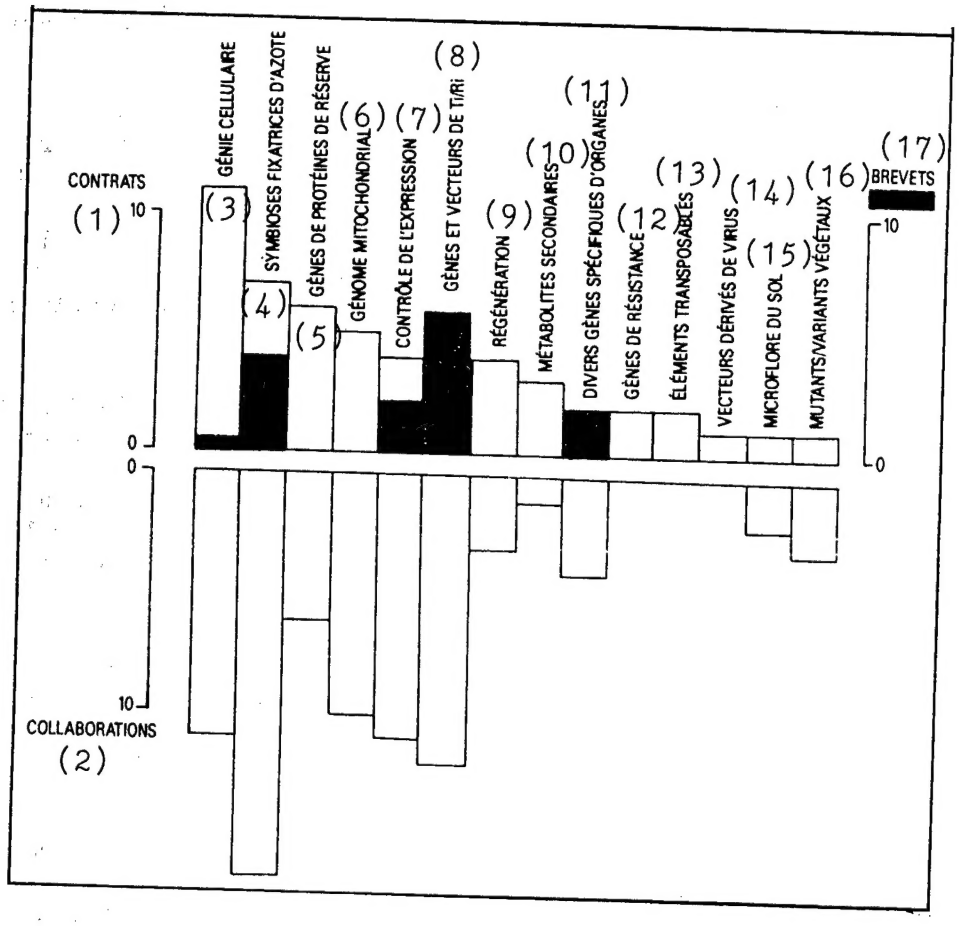


Figure 1. Number of collaborations and patents compared to the number of contracts in each of the 14 specific fields that are subdivisions of the genetic engineering sector for agricultural species

Key:

1. Contracts
2. Collaborations
3. Cellular engineering
4. Nitrogen-fixing symbioses
5. Storage-protein genes
6. Mitochondrial genome
7. Expression control
8. Ti/Ri genes and vectors
9. Regeneration
10. Secondary metabolites
11. Various organ-specific genes
12. Resistance genes
13. Transposable elements
14. Virus-derived vectors
15. Soil microflora
16. Plant mutants/variants
17. Patents

technology themselves or should associate themselves with one of the main expert laboratories. The big expert laboratories meeting on this occasion still numbered only 4, whereas at the end of the program we can count 11 contracting laboratories that have acquired the ability of applying this technology; this may be a way of measuring the progress accomplished in less than 3 years. The number of species that it is now possible to transform by

means of Ti or Ri plasmids has also increased; in addition to tobacco and petunia, it includes species with a definite economic importance, such as potato, tomato, carrot, soybean, alfalfa, clover, beet, rape, asparagus, bulbous Amaryllidaceae, etc.

To succeed in the regeneration of transformed plants, several teams have developed "disarmed" vectors, the T-DNA oncogenes being inactivated or deleted.

In connection with the obtention, sometimes spectacular, of genetically transformed plants, these last years' effort, both within the framework of the Biomolecular Engineering Program and outside of it, was focused mostly on genetic controls of natural transformation by Agrobacterium (see boxed item 1).

In the case of the Ti plasmid in which the oncogenes are well defined, their introduction into the host plant, whether alone or in association, under the control of organ-specific or constitutive promoters, offers a new way toward understanding the hormonal mechanisms that are at the origin of various cellular responses. Some contractors are already working along these lines, searching for genes specifically activated or repressed in the presence of any Ti oncogenes.

While it may seem easy to draw up a list of the advances made in a field as rich in scientific breakthroughs as this one, nevertheless it remains for us to mention a few areas with shadows that do not seem likely to be dispelled in the near future. These are, among others, the host range limitations and the protocols of integration into the plant genome:

- Host range: Although it has been possible to transform certain monocotyledonous plants with Agrobacterium (among Liliaceae and Amaryllideae), no success has been registered with gramineae in spite of the appreciable efforts applied. Various reasons can be presented, such as the non-expression of the marker genes used, the bacterium's inability to adhere to the plant-cell wall, a graminea deficiency in producing substances including virulence genes, or a lack of other unknown factors;

- Protocols of integration into the plant genome: The mechanisms involved are still unknown and the manipulator is limited to observing a certain number of structural or functional absnormalities in transferred DNA without having any real control over these phenomena. For example, the number of integrated T-DNA copies is not well-defined, and above all, transferred-gene expression is not always stable. It has already been possible to observe an inhibition of nopaline synthase or octopine synthase genes, the cause of which was tentatively attributed to DNA methylation or, more generally, to a "position effect" that could modulate the level of introduced-gene expression as a function of localization in the recipient genome. On the other hand, in the form in which it was integrated, T-DNA then goes through meiosis and is transmitted to progeny, apparently without undergoing any other rearrangements.

To conclude this section on the study of Ti/Ri plasmids, it should be noted that the efforts of the Biomolecular Engineering Program contractors in this particular field resulted, in a much shorter time, in tangible achievements

that can be measured by the number of patents or by the large number of cooperation agreements (see Figure 1) for a limited number of contracts (quantitative figures are available for 4 contracts listed in this field); this is the area where the proportion of patents (a total of 6) to the cooperation links with all the other laboratories in the program (a total of 12) is the highest.

In the second part of this article we will present the results achieved on nuclear and cytoplasmic genes, protoplast manipulation and plant regeneration from protoplasts or from free cells.

[Boxed item 1, p 59]

Genes Involved in Natural Transformation by Agrobacterium

Three categories of genes essential to the formation of tumors or of hairy roots have been identified in the bacterium. These are chromosomic genes, virulence genes and oncogenes.

- Chromosomic genes govern the adhesion of the bacterium to the plant-cell wall and contribute to the determination of the host range.

- Virulence genes are plasmidic, they participate in T-DNA transfer to the plant cell and some of them also determine the host range. Some contractors have succeeded in demonstrating that these genes could function in cis or in trans relatively to T-DNA, and that their activity was induced at the transcription level by exogenous factors present in plant exudates or in liquids from wound sites.

- Oncogenes, included in T-DNA, confer to the transformed cells in which they express themselves the ability to grow in the absence of added hormones. In the case of the Ti plasmids, three oncogenes are known and characterized. Two of them (aux-1 [auxin] and aux-2] code for enzymes that catalyse indole-acetic acid production, and the third one (cyt) [cytokinin] for an enzyme involved in isopentenyl-AMP production. In the case of the Ri plasmids, although it has been possible to identify several oncogenes, their functions are ill-defined, and four contracting laboratories will pursue, in the coming years, their analysis of the factors responsible for the aberrant morphogenesis induced by A. rhizogenes.

[June 86 pp 41-45]

Last May, we presented an assessment of the research done in the molecular genetics of various plant-microorganism symbioses and of natural plant transformation by Agrobacterium. Considered as a whole, the symbiosis field ranked among the most active in the program, with the obtention of four patents and a number of collaborations corresponding to more than 2.3 times the number of laboratories involved. The same situation exists in the study of the genetic control of plant transformation by Agrobacterium: six patents (for a limited number of contracts: four) and a large number of collaborations with all the other laboratories in the program. Thus was sketched the formation of a network of relations between laboratories covering multiple fields of

expertise in several EEC member states. With the results achieved in the study of cytoplasmic and nuclear genes and in protoplast manipulation, the concept of "institutes without walls" becomes stronger.

Nuclear genes

Three categories of genes are predominant in the contractors' work, i.e.: families of genes coding for storage proteins in the endosperm of cereals or leguminous plants, genes for resistance (to parasites, herbicides, antibiotics), and various genes whose expression is specific to organs (leaf, root nodules).

Thus, 20 different genes are being studied from the point of view of their molecular structure and their functioning. In this field, research proceeds by steps; first, it involves isolating the gene (boxed item 2), then characterizing it and understanding the control mechanisms of its expression.

It has been possible to undertake gene characterization in a good number of cases where the gene-isolating step had been taken earlier in the implementation of the contracts. Figure 2 shows a schematic representation of the different regions of a gene model on which the participants focused their analysis, regarding its regulation and product synthesis.

From this schematic review of the genes studied within the framework of the program it appears that many differences exist between these gene categories, in the order of essential sequences as well as in the mechanisms regulating their expression. Few general rules seem to apply and each system calls for laws of its own that determine its originality. The system that was the most thoroughly studied by a group of contractors from three different laboratories is certainly the system of genes coding for cereal prolamins. These genes' evolutionary characteristics are such that two domains can be differentiated. The coding sequence specifying the NH_2 end of the protein, constituted of repeated segments, shows a recent evolutionary origin and has determined size increases in the molecule. Toward the COOH end of the protein is located the ancestral domain, non repeated, in which can be recognized 3 different regions of $\pm$40 amino acids, that are common to rape secalin, gliadin, trypsin-inhibitor or 2S storage protein.

Homologous and heterologous expression systems have been developed. They allow to study the functioning of genes situated downstream from promoters that are themselves homologous or heterologous, complete or deleted. Expression systems developed in higher plants are based on expression-transfer vectors derived from Ti [tumor-inducing]/Ri [root-inducing] plasmids. One remarkable result, among several others, is the transfer to clover of a marker gene conferring antibiotic-resistance (CAT [chloramphenicol acetyl transferase] gene) whose expression depends on a soybean leghemoglobin promoter: In clover plants regenerated after transformation, the marker gene expresses itself in the nodules when Rhizobium meliloti is present, but neither in the roots nor in the stems nor in the leaves.

A very special expression system has been developed in wheat, through micro-injection into the coenocytic endosperm of a construct including the marker

CAT gene under the control of various promoters such as that of the cauliflower mosaic virus (CaMV) 35S gene or of the maize sucrose synthase gene. These promoters function in wheat and, as the case may be, conserve their development-related specificity since resistance is expressed only on the 12th day after fertilization in the case of sucrose synthase, whereas it seems constitutive with the CaMV promoter during the whole experimental period.

Heterologous plant-gene expression has also been achieved in the yeast system. Yeast was transformed by a plasmid construct including the fusion of the soybean leghemoglobin gene with a resistance gene (CAT). In this case, not only the gene expresses itself, but its expression is controlled by the ability of the yeast to produce heme molecules, an ability that can be enhanced on a nonfermentative carbon source. Expression regulation of the chimeric gene by yeast heme is post-transcriptional and involves sequences at the 5' end of the leghemoglobine gene.

In another laboratory, it is maize zein that can be expressed in yeast. The plant promoter is recognized by the microorganism, and the level of expression is directly controlled by the growth stage of the culture.

To summarize this field's contribution to the whole program, through the study of either nuclear genes or cytoplasmic genes discussed separately here, we must emphasize its capital importance for future possibilities of genetic engineering applications. Although other related fields--molecular vector development or protoplast manipulation--may claim results, sometimes more spectacular, in a short time, it is nevertheless true that the steady progress of basic research on the molecular biology of crop plants will be a controlling factor in the development of practical applications for genetic engineering tools devised in other parts of the program. The work presented at Wageningen may remind us of the importance that the main nuclear genes described here have for agriculture and for food (see table 1).

From the standpoint of program coordination, this field is shown to be rich in commercially applicable results (patents) and favorable to very strong international collaborations: the number of collaborations is higher than the number of contractors involved.

Table 1. Importance of Nuclear Genes for Agriculture and Food Crops

High-molecular-weight glutenin	→ wheat-flour baking quality
Cab [chlorophyll ab binding protein] transit sequence	→ resistance to herbicides
Unstable alleles at regulation loci	→ maize quality
Grain lectins	→ defense against insects
Endosperm proteins, etc.	→ barley food value

Cytoplasmic Genes

In spite of the fact that cytoplasmic genomes represent only a very minor portion of plant-cell hereditary material, chloroplastic and mitochondrial DNA's control directly, or in cooperation with nuclear DNA as the case may be, a certain number of essential functions that affect plant productivity:

- CO_2 fixation;
- ATP [adenosine triphosphate] synthesis;
- expression of cytoplasmic male sterility (cms);
- resistance to herbicides;
- resistance to diseases;
- reduced growth;
- resistance to drought, etc.

Three lines of research have been followed by contractors in this field, i.e.: structure and stability of chloroplastic and mitochondrial DNAs, molecular bases of cytoplasmic male sterility, cytoplasmic genome manipulation.

1. Structure and Stability Studies

Wheat DNA structure has been described (by a contractor from Orsay, France), and its multiple recombined subgenomic forms, on the basis of 10 repeated sequences in the 430 kb [kilobase] circular molecule, have been well explained. One of these repeated sequences contains the 18S/5S ribosomal RNA genes flanked by single sequences and present in three different loci of the main molecule. They can therefore, through successive crossovers, give rise to nine district genomic-environment combinations on the borders of repeated rRNA [ribosomal RNA] genes that are found again in the subspecies generated by these recombinations of the main molecule. But considering the fact that there is a total of 10 repeated sequences, the number of foreseeable molecular subspecies is very large, which explains the great heterogeneity of mtDNA (mitochondrial DNA) populations, as confirmed, furthermore, by electron microscopy.

The relative stoichiometry of related molecule families seems stable for a given tissue, which then poses the problem of the replication autonomy of each mtDNA subspecies. Are there several points of origin for replication in the main molecule?

Elevent fragments that are capable of autonomous replication (ARS) have been identified in yeast. But are they recognized points of origin for replication in the plant cell? Enlightening information is provided on this subject by studies on Petunia chloroplastic DNA conducted in Amsterdam. This is a 150 kb circular molecule that has been almost completely characterized by another team in the program. It contains 20 genes and 2 ARS and these 2 sequences that are capable of transforming yeast appear actually unable to function as points of origin for replication in the plant.

By contrast, another sequence 1 kb away from ARSb presents all the characteristics of a potential point of origin for replication, by analogy with the sequenced points of origin for replication in Chlamydomonas or Euglena.

Everything leads us to believe that an ARS that transforms yeast is not necessarily a point of origin for replication in the plant cell. It remains to be demonstrated, in the case of Petunia cpDNA (chloroplastic DNA), that the sequence recognized as a possible point of origin for replication is actually capable of retransforming the plant.

2. Molecular Bases of Cytoplasmic Male Sterility

The study of molecular bases of cytoplasmic male sterility (cms) is the second line of research followed. This research is amply justified by the necessity of mastering hybrid production in several species of cereals or leguminous plants.

A direct correlation has now been found between the conversion of a 26K mitochondrial polypeptide into a 24K polypeptide and the degree of cms expression in the broad bean (Louvain-la-Neuve, Belgium). This altered product, which may be responsible for pollen degeneracy, has still to be identified and the cause of this alteration has still to be determined. The variant polypeptide shows a hydrophobicity that could confine it to the inner mitochondrial membrane where it would substitute itself for a membrane enzyme complex. But other scenarios are possible, the existence of a microsporogenesis-specific molecule that could, for example, link itself to the variant polypeptide at the level of the respiratory chain.

As for the origin of the variant polypeptide itself, two hypotheses can be proposed: new nucleus/cytoplasm combinations would induce abnormal mitochondrial recombinations, or a mutation would take place at a specific point in the mtDNA.

3. Cytoplasmic Genome Manipulation

Cytoplasmic genome manipulation is the third branch of these researches. Some successes have been registered in the transmission of cms to rape and tobacco, and of atrazine resistance to rape, by protoplast fusion. Another approach, molecular this time, is on the way to becoming operational: the construction of mitochondrial or chloroplastic vectors, using plasmids, points of origin for replication and promoters identified above as construction material (work in progress in Amsterdam).

Protoplast Manipulation and Regeneration

Three separate but complementary activities have been given preference in this field: isolation and characterization of biochemical mutants, protoplast fusion, regeneration of differentiated organisms from protoplasts or from free cells.

Four groups (Brussels, Harpenden, Pisa, Versailles) have worked more particularly on isolating mutants. The enlargement of the auxotrophic mutant collection, particularly in tobacco, but also in alfalfa, constitutes a significant contribution to the whole sector, in which various kinds of applications can be found for mutated lines: several mutants are affected in amino acid biosynthesis pathways, and their characterization is an important

contribution to the analysis of nitrate assimilation pathways in plants; the characterization of "nitrate-reductase-deficient" mutants is progressing rapidly: It has been possible to assign mutations affecting the molybdenum cofactor to five complementary groups and mutations involving the apoenzyme might be able to enter only into two complementary groups. Being able to have these mutated strains available in a species that, furthermore, regenerates very well and lends itself to very frequent transformations is a great asset for isolating corresponding genes, through in vitro complementation and selection. The isolation of genes coding for Nicotiana nitrate reductase should therefore be within reach. Another role that can be attributed to certain mutants is that of parent-line markers that can later be subjected to genetic transfers and can lend themselves to analysis. But it is unquestionably to mutagenesis and selection methods themselves that these teams have devoted their efforts; they were mainly concerned with problems of efficiency, yields and reproducibility.

Seven laboratories have more particularly studied protoplast fusion methods and their applications to agriculturally significant species (Aberystwyth, Brussels, Cologne, Harpenden, Nottingham, Pisa, Versailles). Asymmetrical fusion has definite advantages: the complete inactivation of the donor genome by gamma rays allows the fusion product to conserve most of the recipient's genetic characteristics, with the exception of some uncertain and very limited transfers of minor elements from the irradiated genome. As in the case of mutagenesis, several teams have worked hard at standardizing methods of fusion, with or without irradiation, at optimizing fusion itself by chemical or electrical means, and at improving the efficiency of heterokaryon selection.

At the application level, combinations tested in fusion occurred between Solanaceae or involved one Solanacea as one of the two parents. Two groups (Aberystwyth, Nottingham) are nevertheless striving to achieve somatic hybridization between leguminous fodder plants, between various species of alfalfa or between alfalfa and clover. In any event, the same thing happens for both fusion and mutagenesis: There are few new products to be numbered in those fields; it is rather the methods that were the object of contracted research, and these methods have reached such a level of refinement and standardization that in the future they should no longer present any major obstacle to plant cell manipulation. The obstacle is unfortunately too well known, it always occurs downstream from these manipulations: it is the absence, or the extreme difficulty, of regeneration in many crop plants (boxed item 3).

No truly innovative approach has been suggested in this important field, which calls for renewed efforts in molecular biology and in development physiology. The best hope might be provided by other fields in the program, the field of Ti/Ri plasmids whose now-available oncogenes have the capability of activating or inhibiting characteristic morphogenetic programs, also the field of plant/bacteria interactions, at the interface of which are isolated some active molecules that determine, directly or indirectly, a whole range of cellular responses in the host plant. Within the framework of this program, the field relating to protoplast manipulation has not been the most productive in terms of patents and publications, and the rate of established cooperations per laboratory remains close to 1.0, appreciably less than for the other two fields mentioned above: Ti/Ri plasmids and plant-microorganism relations.

Conclusion

This article concludes an incomplete review that is definitely biased by the partiality of the author's feelings, but one key idea should be remembered from it: Some teams have learned to work together and have been stimulated by the results achieved jointly. Their efforts are teaching us that agricultural-production systems are true biological machines provided with multiple levers that technicians will some day know how to grasp and to control.

Agricultural biotechnology will be the factory in the field, the plant as a factory, the soil as a factory. The main socioeconomic partners of the agricultural sector are not unaware of this. They should not be unaware either of what such a community platform for molecular biology research can bring them in terms of intellectual resources, know-how assets and bases for innovations. TOGETHER AND DIFFERENTLY: This also means bringing the development partners together within the network of contractors involved in the Biomolecular Engineering Program and in the program that is already following it in the field of Biotechnology.* The first ones to enter into the network will probably be the seed companies whose presence at the Wageningen meeting was an event in itself.

[Boxed item 2]

Isolation of Nuclear Genes

Several isolation strategies have been used by the contractors:

- The majority of them, particularly those who work on endosperm storage proteins, have been able to reach the genes by using cDNAs [complementary DNA's] as molecular probes. It was possible to clone these cDNA's because of a knowledge of the gene product that is abundantly present in the grain;

- As for barley chymotrypsin-inhibitor genes, ferrodoxin genes and cytochrome C genes, other contractors have used synthetic oligonucleotide probes, constructed from the NH_2-terminus sequence of the protein when it is known;

- Some have used heterologous probes for sufficiently conserved genes, such as alcohol dehydrogenase in Arabidopsis or for genes coding for chloroplastic proteins in barley, this latter method allowing a rapid probing of the genomic data banks of new species.

If the gene product is not known, and provided that its phenotypic effect can be perceived, there are still other isolation strategies available among the researcher's resources. One of them consists in isolating transposition mutants whose altered phenotype is a result of the insertion of a known transposable element into the gene region under consideration. This approach has allowed the selection, in maize, of four characterized mutants at the opaque locus 2 (controlling grain storage-protein synthesis) and candidate mutants at the dull locus and at the amylose-extender locus (controlling

* Biotechnology Research Action Program adopted by the Council for the 1985-1989 period, which provides for the continuity and amplification of the Biomolecular Engineering Program (see Biofutur, April 1986).

amylose synthesis in grain). One of the 02 mutants expressed an mRNA [messenger RNA] presenting a homology to the transposable Ds [Dissociation] element probe, and all four show the presence of Ds in their vicinity. This, therefore, paves the way to isolating the opaque gene 2 in a very short time.

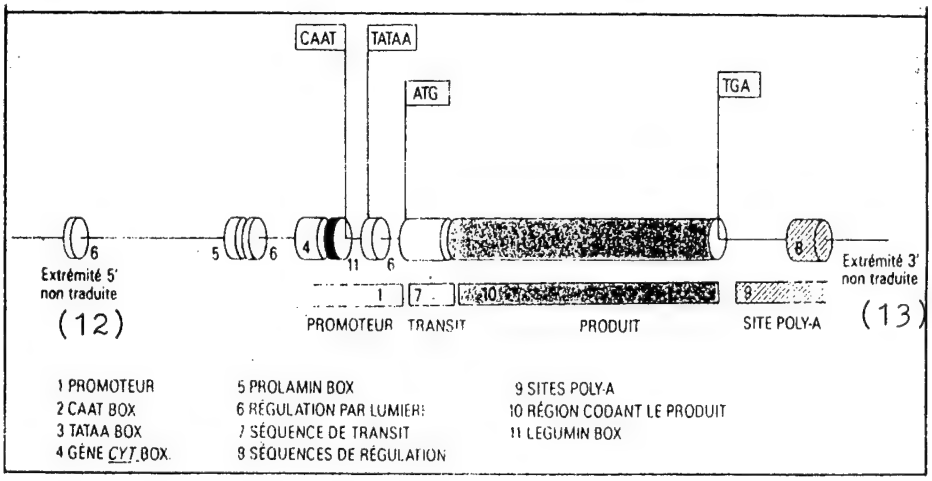


Figure 2. Location of Essential Sequences in a Gene Model

Key:

1. Promoter
2. CAAT box
3. TATAA box
4. cyt [cytokinin] gene box
5. Prolamin box
6. Light-induced regulation
7. Transit sequence
8. Regulation sequences
9. Poly A sites
10. Region coding for the product
11. Legumin box
12. 5' nontranslated end
13. 3' nontranslated end

- Region 1: This is the promoter, which is isolated and characterized in the case of several mono- and dicotyledonous plant genes, as well as for the Ti plasmid genes of Agrobacterium and cauliflower mosaic virus. Promoters have become a much sought-after commodity, particularly those that give the gene a tissue specificity or place it under the control of external physio-chemical signals.

- Region 2: The frequently observed CAAT sequence does not exist in the pea legumin gene and its presence is not essential to the expression of the T-DNA [transferred DNA] cyt gene; in monocots, this sequence is sometimes replaced by another CATC tetranucleotide (barley B1-hordein, wheat α-gliadin).

- Region 3: In all cases described, the TATAA sequence is located approximately 35 bp [base pairs] upstream from the transcription initiation point.

- Region 4: The region located from 130 to 180 bp upstream from the coding sequence is essential to the expression of the T-DNA cyt [cytokinin] gene.

Region 5: All prolamins present a 25-30-bp-long essential sequence approximately at position -300, including a perfectly conserved TGCAAAG heptanucleotide; this sequence could play a role in the coordinated induction of prolamin genes during endosperm development.

- Region 6: Genes whose expression is light-regulated, such as ssRuBPCase (small subunit of ribulose biphosphate carboxylase or Cab (chlorophyll ab binding protein) have control regions located at positions -2/-35, -300 and -700, in tobacco.

- Region 7: Transit sequences have been identified in several genes (RuBCase, B-hordein, chymotrypsin-inhibitor); their role is to contribute to the membrane transport of polypeptide products acting within isolated cell compartments.

- Region 8: Between positions +928 and +996, near the poly A sites, there is a region that is essential to the expression of the T-DNA cyt gene: a regulator element is also present near the poly A site of the Hor 2.4 (B-hordein) gene.

- Region 9: These are the poly A sites that, in the case of maize glutelin or of Petunia chalcone synthase, can be multiple, although the presence of a second poly A site does not appear necessary to gene expression.

- Region 10: This is the region that specifies the product; no intron has been found in storage-protein genes, some have been shown to exist in pea legumin genes, in Petunia chalcone synthase genes and in Arabidopsis alcohol dehydrogenase genes. The legumin gene isolated in the pea presents a peculiarity: the maturation of its mRNA gives rise to the synthesis of two different products.

- Region 11: A highly conserved 28-bp sequence is characteristic of legumins and perhaps of the storage proteins of leguminous plants in general.

[Boxed item 3]

Regeneration from Protoplasts

From protoplasts, a complete regeneration into new-formed plantlets is now possible, with an acceptable frequency, in clover, tomato, rape, chicory, potato, but difficult--if not impossible--in sunflower, Italian rye grass, in all cereals tested and in most leguminous plants. Greater success might be achieved in the regeneration from cells in liquid suspension, particularly when dealing with so-called "embryogenic" lines, as in the case of clover, rye grass and fescue, rice and rye.

12260/9716
CSO: 3698/533

BRIEFS

FIAT FIRM-BOLOGNA UNIVERSITY RESEARCH AGREEMENT--Telettra (a Fiat Group company) and the University of Bologna have drawn up a cooperation and research agreement for the information technology, microelectronics, and telecommunications sectors. This agreement, which will involve the Department of Information Electronics of the University, was signed by Fabio Roversi Monoco, chancellor of the University of Bologna, and Guido Vannucchi, the president of Telettra. The agreement will open up interesting prospects both in terms of the topics that will be considered and because it will try to make the relationship between the university and production system much closer and more efficient; it will also keep technicians and researchers up to date and will improve the preparation of university students. Within the framework of the scientific cooperation agreement, Telettra will also finance annual scholarships for young graduates to be used abroad. Furthermore, the company has indicated its willingness to admit to its research and development labs those students who want to receive training or guidance in academic matters. [Text] [Bologna IL RESTO DEL CARLINO in Italian 12 Jun 86 p 2] 8610/12232

CSO: 3698/M170

OLIVETTI RAISES CAPITAL FOR $115 MILLION

Ivrea NOTIZIE OLIVETTI in Italian Apr 86 pp 4,5

[Text] The largest-scale financial operation ever undertaken by the Group was approved by a special meeting of the shareholders at Ivrea. The operation is designed to raise the corporate capital to a maximum of 40 million nonconvertible savings shares in connection with a bond issue, in Swiss francs, by Olivetti International (Luxembourg), for a countervalue of around 430 billion lire.

The capital-increase operation entails the relinquishing of their option rights by Olivetti's present shareholders, who, however--like the bearers of Olivetti 13-percent convertible 1981-1991 bonds and the holders of Olivetti 1982-1987 warrants--will nevertheless have preemptive right of subscription to the bonds. With a view to placing shareholders residing in and outside of Italy on an equal footing, the former have been permitted to subscribe to the Olivetti International foreign currency bonds without having to effect prior deposit; this marks an absolute first with regard to shares of a private industrial group.

The operation, which closed on 16 April, consists of the issuing of 524,620 bonds having a face value of 1,000 Swiss francs each, for a countervalue of approximately 430 billion Italian lire. Interest is fixed at 3.50 percent and the maturity is 10 years. The subscriber is entitled to one bond in Swiss francs for every 1,000 shares held. Commensurate ratios are provided for the convertible bonds and warrants in circulation.

Each new bond is accompanied by an Ing. C. Olivetti & C., S.p.A. warrant entitling the buyer of the bond to purchase, within a period of 3 years, 40 nonconvertible savings shares of new issue by Ing. C. Olivetti & C., S.p.A., at a preset unit price of 8,375 lire. This price represents the average of the quotations on the Milan Stock Exchange from 10 to 14 March 1986 plus 5 percent.

The new bonds and attached warrants will be listed immediately on the Luxembourg Stock Exchange and thereafter on the Zurich, Basel, Lausanne, Berne Exchanges and on the Italian Stock Exchanges in Milan, Turin, Genoa and Rome.

The financial operation deliberated by the shareholders meeting falls in with the company's strategy of choosing the most favorable moments and most advantageous terms and conditions for seeking the financial resources needed for investments connected with the growth of the Group on the basis of a balanced ratio between its own and third-party funds. The meeting also provided an opportunity to disclose the preliminary estimates of the results obtained by the Olivetti Group and the Group's parent company during 1985; these results will be submitted to the forthcoming regular meeting of the stockholders for examination and approval. The Group's consolidated billings for the year totaled over 6,130 billion lire (up 34 percent over 1984), and those of the parent company 3,487 billion (up 36.6 percent). Net profit for the Group's operations in 1985 totaled approximately 500 billion lire, and that of the parent company approximately 330 billion. The Group's net financial indebtedness as of yearend 1985 was less than 250 billion lire, as compared with 319.3 billion as of yearend 1984. The parent company shows current assets totaling 160 billion lire, versus 100.8 billion as of yearend 1984.

In 1985, some rather substantial investments were made in fixed and commercial assets (490 billion for the entire Group) and in research and development activities (280 billion).

9399
CSO: 3698/473

BELGIAN SUBMICRON, AI PROJECTS IN EUREKA

Amsterdam COMPUTERWORLD in Dutch 15 Apr 86 p 5

[Article signed J.S.: "Participation of Belgian Companies in EUREKA Projects Extended"]

[Text] Brussels--The number of Belgian companies taking part in the European EUREKA project has again risen.

The Flemish UCB [Belgian Chemical Union] company, the Interuniversity Microelectronics Center (IMEC) of Louvain, and a British company are going to conduct a joint project for the development of a procedure based on photolithography to produce submicron-level integrated circuits. Submicron-level technology is used in the production of memory circuits of 1 megabit or more.

MOSES

Furthermore, Belgian companies will be integrated in the so-called MOSES project for the development of a multimedia information system and in a program for the development of a management system for large industrial projects based on artificial intelligence.

The EUREKA Steering Committee has added the above-mentioned projects to the already existing list of EUREKA projects. On 30 June, the London conference of EUREKA ministers must consider and approve the complete list.

In the meantime, the Belgian Ministry for Scientific Policy has installed a data bank which includes all Belgian and foreign companies participating or interested in participating in EUREKA. For further information please contact the Dienst voor programmatie van het Wetenschapsbeleid [Scientific Policy Planning Department], Wetenschapsstraat 8, 1040 Brussels.

25006/9274
CSO: 3698/A129

EEC INVESTMENT IN ESPRIT, OTHER R&D DEBATED

Amsterdam COMPUTERWORLD in Dutch 15 Apr 86 pp 20, 23

[Article by Jan Schils: "EEC R&D Expenditure Under Pressure"]

[Excerpts] Luxembourg--The last meeting of the EEC R&D ministers revealed that the serious problems confronting the European budget threaten to have a negative influence on R&D expenditure for the period between 1987 and 1991, which was set at 25 billion guilders by EEC Commissioner Karl-Heinz Narjes in his second overall program.

This expenditure should mainly benefit information technology and telecommunications, thereby improving the competitiveness of EEC countries against the United States and Japan.

In Luxembourg the R&D ministers, presided over by Minister of Economic Affairs van Aardenne, held a first discussion on this overall program. It became clear that the majority of the EEC countries are not willing to spend 25 billion guilders on technological research and the development of products based on new technologies when this year's EEC budget already has a projected deficit of nearly 10 billion guilders.

In any case countries such as the UK and the FRG, which have a decisive vote, considered this amount too large, and even the Netherlands, which gives high priority to EEC policy concerning new technologies, seemed in Luxembourg to have some reservations about the 25-billion guilder amount cited by Narjes. Our country would prefer an amount ranging between 17.5 billion guilders and 20 billion guilders.

The EEC Council of Ministers highly praised the ESPRIT program, which had a very successful start. This joint European program emphasizes cooperation on information technology. Experts from the member countries have recently expressed their satisfaction with the program.

Consequently, the European Commission proposed that the Council of Ministers raise expenditure on the ESPRIT program (included in the second overall program) by 300 percent and earmark 5.5 billion guilders of the European budget for that purpose. The European Commission would like small- and medium-sized companies to be more involved, especially in the ESPRIT program.

No concrete decisions were reached in Luxembourg concerning the second overall program. It is obviously still too early for that, because the European Commission published this R&D program for the 1987-1991 period only 4 weeks ago.

Against the will of the European Parliament delegation, the Council of Ministers promptly halved the research budget for advanced and raw materials.

Instead of 500 million guilders, this program received "a mere" 275 million guilders from the European budget.

Overlapping Research

Finally, the European Research Council revealed once again that a growing number of delegations are convinced of the need to stop the substantial amount of overlapping research conducted within the EEC, which is chiefly caused by national pride. This conviction is gaining ground now that the EEC budget is facing deficits.

The decision to give the GCO's [Joint Research Centers] no more funds for the next 4 years than they received for the previous 4-year period (1,680 million guilders) should also be interpreted in this context. This implies that wages of the very well-paid officials in Ispra and Karlsruhe will rise a little slower. Major cuts could be made, particularly in Ispra, where over 1,600 people are employed. The remaining GCO's (Petten, Karlsruhe, and Geel in Belgium) employ 520 people and their net results are relatively better.

25006/9274
CSO: 3698/A129

THIRD WORLD COUNTRIES BUY SWEDISH NUCLEAR WEAPONS TECHNOLOGY

Stockholm NY TEKNIK in Swedish 2 May 86 pp 12-15

[Article by Christer Larsson, Jan Melin: "Here's Where Sweden Sells Nuclear Weapons Technology"]

[Text] Sweden for many years has been producing and exporting advanced technology for the manufacture of nuclear weapons. This involves military flash X-ray devices which can transilluminate anything from high-explosive shells to sensitive nuclear weapons tests. The machines are exported under conditions of great secrecy to the high commands of the armed forces in Pakistan and India, among other places. But also Israel and South Africa have received machines from Sweden. These are countries which already have or are very close to having fully developed arsenals of nuclear weapons. Now the Swedish Government is to decide the issue of a new large export of machines to India, machines which run the risk of going straight into the country's underground nuclear weapons program.

The Swedish export of more or less obvious nuclear weapons technology is occurring at the same time as Sweden is officially pursuing an international arms reduction policy in order to prevent further nuclear weapons proliferation.

Now the armed forces of India are asking to be allowed to buy additional sensitive so-called dual-use technology from Sweden. These are products which, according to Swedish law, are of "decisive significance for the production of nuclear weapons."

Among other things, this includes military flash X-ray machines. These are very powerful machines, which in a fraction of a second develop a huge electric pulse of up to 10 billion watts. It is done by discharging a series of very powerful condensers.

Ten million watts is as much as 20 medium-sized power plants generate together. With that output, one can transilluminate anything from high-explosive shells to advanced nuclear weapons tests. Flash X-ray machines, as a matter of fact, are a key resource in all nuclear weapons programs.

In Sweden these systems were developed originally by the FOA [National Defense Research Institute]. It was for the Swedish nuclear weapons program during the 1960s, but also for conventional projectile tests.

It was when the Swedish nuclear weapons program was dismantled that the patent and production rights were transferred from the FOA to the newly formed company AB Scanditronix in Uppsala. That occurred in 1968. From this company the daughter company Scandiflash was later formed.

Behind Scanditronix and the arrangement with the FOA stood Curt Mileikowsky, the former head of SAAB [Swedish Aircraft Co]. Via Mileikowsky the machines were developed into an exclusive, controversial, but very profitable export business. For several years, Curt Mileikowsky has also been sitting on the FOA board of directors. Several attempts have been made at a high level to remove him from the board. But without success.

The attempts to get Mileikowsky out have been made because the FOA has a discreet but important role with regard to controlling the flow of nuclear weapons technology to Pakistan, India, Israel, and South Africa, among other places.

Straight Into India's Nuclear Weapons Program

These are the same countries whose military authorities are major customers of Scandiflash--the concern which was started through cooperation between the FOA and Mileikowsky, and in which Mileikowsky continues to be a partner. So now India is asking to be allowed to buy three of the largest flash X-ray machines--the 1,200-kV size--from Scandiflash. The output from a machine this size is 10 billion watts.

For all exports of machines with voltages over 500 kV, an export license from the Government has been required since 1984. This is based on the intimate connection between flash X-ray machines and nuclear weapons development. But up to 1984 this export was completely unregulated from Sweden. It had then been going on for nearly 20 years. The SKI [Swedish Nuclear Power Inspection Board] is now making a stand against the requested export to India.

The SKI says that the Swedish equipment runs the risk of going straight into India's nuclear weapons program.

The application which now is to be dealt with comes after a previous unsuccessful attempt to export the Swedish equipment via British intermediaries. That was last year. At that time the Swedish Government granted an export license to the firm of Hadland Photonics Ltd in England, for further export.

Behind Hadland stood India's Ministry of Defence as the buyer. This is confirmed by Terry Johnson, president of Hadland Ltd today. The fact that the deal nevertheless did not come off is due to the fact that the British Government in the end refused to allow the equipment, which in their eyes was strategic, to be sent on to India's armed forces.

Scanditronix, and later Scandiflash, are thus the commercial extension and continuation of the Swedish nuclear weapons program which began to be dismantled in 1968. At that time the Government declared officially for the first time that Sweden had decided to forgo nuclear weapons of her own. Otherwise, in a short time the country could have gone the full course and joined the other nuclear weapons powers.

No Governmental Restrictions

In 1970 Sweden signed the so-called NPT [Non-proliferation Treaty]. It prohibits both a country's own nuclear weapons development and the export of sensitive nuclear weapons technology. However, the government approves the continued export of the sensitive machine by Scandiflash. No export restrictions are laid down. This means that Scandiflash is developing into one of the world's leading producers of these extremely specialized machines. Among other producers are Hewlett Packard in the United States and Société de Verrerie et Thermométrie in France.

But with this, Scandiflash has also become established in an extremely risky and distorted market. Among the other actors in this market were a number of more or less sophisticated dummy firms, as well as the intelligence and security services of the superpowers. Nine customers out of ten are military agencies. Most of them need flash X-ray machines for conventional ammunition programs. But during the 1970s a new market came into being.

At that time Israel had already established itself as an unofficial nuclear weapons market in the Middle East. In 1974 the world was shaken by an Indian nuclear weapons explosion. This in its turn put momentum into new nuclear weapons programs in other countries. One of the countries that felt most challenged was India's neighbor country Pakistan.

Six years later, in about 1980, Pakistan had procured for itself a significant plant program for nuclear weapons production. According to American sources, developmental work took place in the area of ignition mechanisms and other key components. They formed the series of devices which were required to initiate the final nuclear weapon detonation. In 1982 Pakistan turned to Scandiflash in Uppsala with a large order for heavy flash X-ray machines.

It included three 450 kV systems and six 1,200-kV systems, the firm's largest machines. Appearing as the buyer was Pakistan Precision Engineering Complex Ltd. It is formally a daughter company of the state airline company PIA [Pakistan International Airlines]. But according to Indian intelligence sources, it is connected to Pakistan's Ministry of Defense, and thus is accessible for the underground nuclear weapons program. In November and December 1982, the nine flash X-ray devices were shipped out of Sweden.

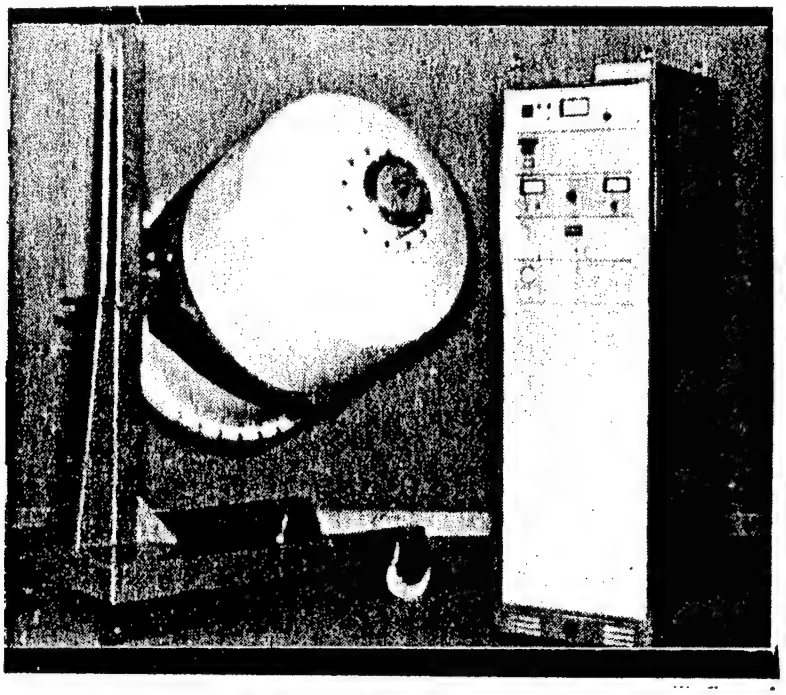
The export was noted by the American intelligence service. An attempt was made there--but in vain--to halt anything that could have the least connection with the Pakistani nuclear weapons program, among other things.

Earlier the same year, the United States had succeeded in putting a stop to a significantly smaller export of flash X-ray machines from Hewlett Packard to Pakistan. It was possible to do this by means of a battery of various legal clauses and export control regulations which have existed for a long time in the United States.

But in Sweden there did not yet exist any legislation on nuclear technology in 1982. In the same year, 1982, two 1,200-kV machines were shipped to the Soviet Union.

The United States now made new contacts with Sweden and asked for prompt and powerful measures to dam up the sensitive but freely flowing export. Since 1979 a government commission of inquiry had been working to look through the whole area of nuclear export. While the commission was working on legislation on nuclear technology, the American efforts to influence the Swedish authorities continued.

Among other things, the United States did not want Pakistan to receive help in installing and adapting the nine systems which had already been exported there. Installation and onsite testing was included in the contract with Scandiflash.



This 1,200-kV flash X-ray device has been exported to several prospective nuclear-weapons countries.

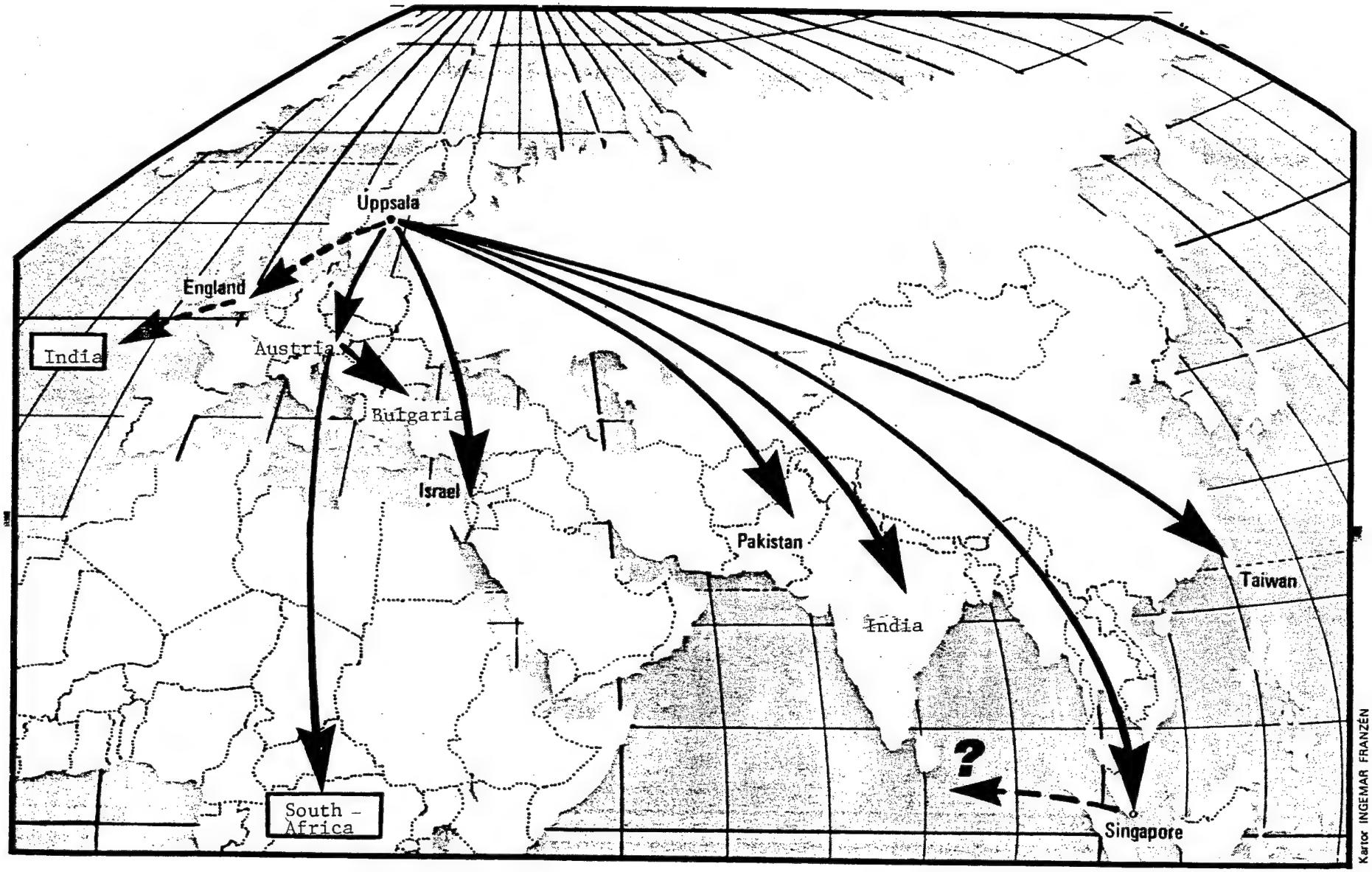
They Forced Us to Wriggle out of our Undertakings

But the company management yielded. It happened after repeated warnings from the FOA, which had significant opportunities to influence the new legislation which was on the way.

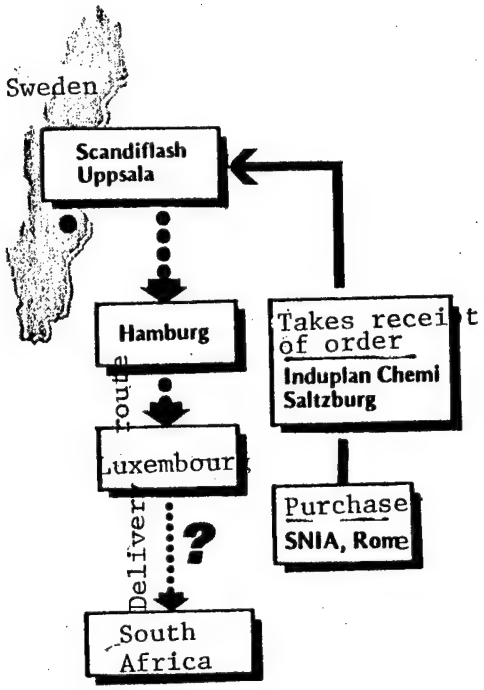
"They forced us to wriggle out of the installation work we had undertaken to do," Scandiflash president Arne Mattsson says today. "The United States just has to blink, and our authorities lie down."

In 1985, 3 years after the Swedish flash X-ray devices had landed in Pakistan, the American intelligence service CIA reported that Pakistan had made a successful test explosion with a complete nuclear weapon ignition. This was interpreted to mean that Pakistan had constructed a scale model of a nuclear weapon, fitted it with nuclear weapon electronics, and test-exploded the whole thing with conventional explosives.

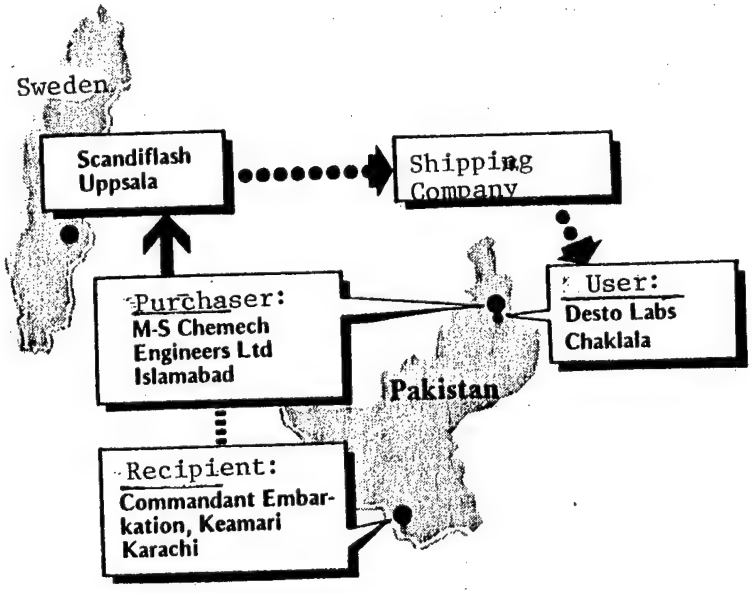
In order to study the extremely rapid processes that occur inside a nuclear device, one or more flash X-ray machines are required. They can trans-illuminate from a distance the two explosion chambers, the outer shell of steel, and the inner shell of lead, to see the details in the explosion process. The exposure time is lightning-fast: 20 billionths of a second.



This is the riskiest export of flash X-ray machines from Sweden. The shaded countries are the most controversial, since they are classed as risk countries in connection with nuclear weapons. Bulgaria, Austria, Singapore, and Taiwan are known for extensive technology smuggling.



From Sweden to an unknown destination via Frankfurt and Luxembourg. Several indications suggest that the Swedish machines went on to South Africa.



From Sweden to the Defense Research Institute (Desto Labs) in Pakistan. The purchaser was a civilian firm in Islamabad.

Swedish Machines Prerequisite for Pakistan

Detailed knowledge of the ignition processes is essential for Pakistan for two reasons: partly to maximize the yield of the devices that are planned and partly to achieve such a high level of sophistication that Pakistan in the end will not need to do any full-scale nuclear weapons tests. Such a test explosion would be immediately detected and would risk a violent reaction in the world around Pakistan, not least in the neighbor country, India. This is how Israel went about it. The fact that Pakistan has chosen the same path can be inferred from a number of American sources which specialize in the subject.

This means that one of the central prerequisites for this path may be the heavy flash X-ray machines which Scandiflash delivered from Uppsala already in 1982. Few persons outside Pakistan today know with certainty where these systems are installed.

In 1984 came a Swedish law on activity in nuclear technology. It introduced forcible measures to limit the outflow of Swedish so-called dual-use technology: equipment that can be essential for production of nuclear weapons. This means, among other things:

1. Flash X-ray Machines with a voltage above 500 kV. This is an adaptation to what is found in the world around. Produced in Uppsala.

2. Hot Isostatic Presses. Can be used to press special explosives for nuclear weapons. Produced by ASEA [General Swedish Electric Co]. Have been exported to South Africa and India, among other places.

3. Neutron Generators with special performance characteristics. Another FOA product for the Swedish nuclear weapons program. No longer produced in Sweden.

Customs was given the complicated responsibility of checking that these, and a long string of other products in nuclear technology, are not exported from the country without a permit.

But customs was not given any reinforcement or any competence in nuclear technology. That competence is found rather within the American intelligence agencies. Scandiflash caught their eye once upon a time, and now they follow the firm's contacts in the world around us. Particularly in India and Pakistan. Information which now and then is passed on to Swedish authorities.

"Someone has been tasked to keep watch on us," says Arne Mattsson, president of Scandiflash. "This is the case particularly in one of our customer countries. Every time I come home from there, I get a call from Swedish authorities who ask questions about what I have been doing."

What happened, then, when the new law on nuclear technology became effective in February 1984?

--September 1984: The Government granted an export permit for a 600-kV flash X-ray machine to the Bulgarian Ministry of Machine Building. The Government thought it had been given guarantees that the system would remain in Bulgaria. The country is notorious as a transit point for sensitive technology.

Export to International Weapon Smugglers

--December 1984: Scandiflash exported a double 450-kV (two-channel) flash X-ray machine to Singapore. They were able to do it without a license since the system was below the permit limit of 500 kV.

The purchaser was Chartered Industries of Singapore Ltd. This is the same firm that figured in a large suspected smuggling of Robot 70 [RBS 70] missiles from Bofors to Bahrain and Dubai.

--April 1985: Scandiflash flew out 2.9 tons of flash X-ray devices to Israel. This involved a half dozen machines rated at 300 and 450 kV. The consignee was the firm of Weissman & Lewy Ltd in Tel Aviv. For obvious reasons, Israel has never signed the non-proliferation treaty (NPT). This is because the country, by all accounts, has a significant arsenal of nuclear weapons.

--Autumn 1985: Scandiflash exported spare parts for previous machines that had been delivered to India, along with a new 300-kV machine for a military research institute in India. As a result of this, the machines became accessible for any desired purpose in the Indian armed forces.

--November 1985: The Government granted an export license for two 600-kV machines for the Italian firm of SNIA in Rome. This is one of Italy's largest war-materiel and nuclear-technology firms.

To South Africa Via Frankfurt and Luxembourg

What the Swedish Government overlooked when Minister of Energy Birgitta Dahl granted the export license was that the same company figured in an extremely mysterious and hitherto unexplained export deal in 1980.

It involved two 1,200-kV and two 300-kV machines, these too from Scandiflash in Uppsala. Everything was ready for transport to Rome in August 1980. It was the culmination of a long negotiation procedure which had started long before.

But at the same time as the systems were beginning to be loaded, a new firm was suddenly introduced into the deal. It called itself Induplan Chemie [Induplan Chemistry] and was located in Salzburg, Austria. Induplan Chemie stated that it was taking over the purchase from the firm of SNIA. At the same time, the request was made that the machines should be flown to Frankfurt am Main instead of Rome.

Within Scandiflash the deal was redirected, accompanied by increasing amazement. Salzburg or Vienna would have been more natural. When the heavy machines were landed in Frankfurt, the deal with Scandiflash was concluded.

Now the systems were redirected once more by Induplan Chemie. This time to Luxembourg. The little grand duchy scarcely has need of any flash X-ray machines. Least of all, ones of the caliber that is especially interesting in a context of nuclear weapons.

Rather, South Africa has this need. Several signs point unambiguously in that direction and no other. The fact that South Africa today is close to its first fully developed nuclear device is confirmed by a whole string of specialist sources.

This means that South Africa is a country for which flash X-ray machines are a necessity. A number of circumstances now suggest that the South African nuclear weapon program, via intermediaries, obtained its machines from Scandiflash.

--December 1985: Time for the next export merry-go-round. A smallish engineering firm in Pakistan, M-S Chemech Engineers Ltd, ordered six 450-kV machines. The firm is located in Islamabad. For some reason, the firm was acting as agent for a Pakistani army agency outside the metropolis of Karachi. The army stated that it was the consignee. Via Hamburg and Karachi, the six Swedish flash X-ray machines were routed to the garrison town of Chaklala, outside Islamabad.

The machines were unloaded at something called Desto Labs. According to the telephone directory for Islamabad, "Desto" stands for Defense Science and Technology Organization.

It is the research institute of the Pakistani armed forces, and is directly subordinated to the Ministry of Defense. It is also directly connected to the underground nuclear weapons program. That makes the Pakistani Ministry of Defense one of Scandiflash's largest customers, with purchases of at least 15 systems rated from 300 to 1,200 kV. According to an American intelligence report, which leaked out last year, Pakistan today is 1-2 years from its first fully developed nuclear device.

Within the Pentagon and the American State Department, further restrictions are now being contemplated on exports in the area of nuclear technology.

New Restrictions Could Mean End of Scandiflash

In those circles, there is very great irritation with the continued Swedish export of flash X-ray devices to the countries on the nuclear-weapon threshold.

Further restrictions can mean the end for Scandiflash, which only has this one product. It would also mean the end for the remnants of the Swedish nuclear weapons program. Remnants which for 20 years may have made active contributions to the underground nuclear weapons programs in Pakistan, India, Israel, and South Africa. It was possible for this to happen without Scandiflash's having stepped beyond the bounds of the new law on nuclear technology one single time. After all, the entire area was completely unregulated in Sweden up to 1984. Within a short time, the new law is now to be tested on a large scale. Three of the largest flash X-ray machines, rated at 1,200 kV, are involved.

Affects on Sweden's Credibility in Disarmament Context

"There is no doubt that these machines are primarily of interest in the context of nuclear weapons," says a highly placed source at the FOA. The purchaser is India's Ministry of Defense. As a result, the systems are accessible for any purpose desired.

Several indications suggest that this request is connected to the large multibillion-kronor deal between India and Bofors, which now is theoretically ready to proceed. People at the Swedish Ministry of Industry are saying "the Ministry of Foreign Affairs can comment on that." At the Ministry of Foreign Affairs, they are declining to comment on the matter.

At all events, India has made it clear that a positive decision is expected there in the Scandiflash matter. Because India has few alternatives. As a result of her demonstrative nuclear weapon explosion in 1974, India is effectively blocked in the United States from anything that has the least little bit to do with nuclear weapons.

The anticipated decision by the Swedish Government in the matter of India therefore will have an influence on everything Sweden has in the way of credibility in the disarmament context.

This is How Flash X-ray Device Works

Flash X-ray devices [FXDs] are used primarily in weapon development, both for nuclear weapons and conventional weapons.

What distinguishes a flash X-ray device from an "ordinary" X-ray unit, which is used in medical care, for example, is that the flash X-ray device develops a much larger output in a very short time period.

When a FXD is used, one places what one wants to study between the FXD and the camera that is to record the course of events: an explosion, for example. Explosions form large gas and dust clouds around the point of burst.

X-ray

To see through this cloud, X-ray study is required. To protect the X-ray equipment, a protective barrier is required: thick steel, for example. Very high outputs are needed for the X-radiation to be able to force through the steel barrier. A large FXD may develop outputs of above 10 GW (10 billion watts), which correspon-s to the combined output of 20 medium-sized nuclear power plants.

The output is developed over a very short time: about 20 ns (20 billionths of a second). The short pulse time is important because the processes people want to radiograph go enormously quickly: for example, the shock wave that results from an explosion.

Simulated Explosion

It is not only explosions that can be studied with a flash X-ray device. One can also get a peek at what happens when a shell penetrates various materials, or how the shell's fuze behaves.

When FXDs are used in nuclear weapons development, it is not only the nuclear explosion itself that one studies. Such an event is impossible to radiograph because the X-ray equipment would then literally burst into atoms. What one examines is a simulated nuclear explosion in which the fissionable nucleus--plutonium, for example--is replaced with a lead nucleus. But even a simulated nuclear explosion requires thick protective barriers to protect the X-ray equipment.

Shrinking

Then relatively powerful FXDs are required. One can also scale down (shrink) the simulated nuclear explosion. Then one can get by with a less powerful FXD. But it is not only the penetrating power of the X rays that determines how much information one can read from a radiograph. With today's enormously rapid development of digitized image analysis and image processing, one can now read more information from an X-ray picture than was possible just a few years ago. Or, as the inventor of the Swedish FXD expresses it, "With computerized image processing, a skilled physicist can test a great deal even with a small FXD."

Export With No Rules Up To 1984

In 1984 came the law intended to halt the export of flash X-ray devices.

It is called the "Law on Activity in Nuclear Technology," and it is aimed at "making it possible to fulfill the obligations ensuing from Sweden's agreements to the end of preventing the proliferation of nuclear weapons."

The obligations referred to were incurred when Sweden signed the treaty on the non-proliferation of nuclear weapons (NPT) which was concluded in 1968. With that, Sweden undertook not to export products which can contribute to other countries' developing nuclear weapons.

The Government bill on nuclear technology states that the export control should be limited to a small number of well-defined products. This is so that it will be possible to have an effective control. The products covered by the law "shall have decisive significance for the production of materials for nuclear devices."

No Obstacle

The products that the Government wants to control are listed in a special annex. Included here as a special item are flash X-ray devices larger than 500 kV. The law came out in 1984. Thus, up to then there was no obstacle to exporting even the largest flash X-ray devices from Sweden.

Robert Nilsson, who developed the Swedish flash X-ray device, says, "it strikes one as old-fashioned to set a limit at 500 kV for when a flash X-ray device becomes interesting for nuclear weapon research. I think it is enormously difficult to set any kinds of limits."

The normal process when one wants an export permit for flash X-ray devices larger than 500 kV is this: The application is sent to the SKI [Swedish Nuclear Power Inspection Board], which makes a judgment: Partly on whether the recipient can be suspected of being engaged in activity in nuclear technology, partly a general judgment of the country of destination. For example, whether it has signed the NPT, etc.

The SKI report then goes to the Ministry of Industry, which consults with the Ministry of Foreign Affairs and the National Defense Research Institute about the suitability of exporting. But the Government has the option of permitting export even if, for example, the SKI recommends rejection of an application for export. For, as it says in the government's bill on nuclear technology, "Above and beyond considerations of the non-proliferation type, the government naturally has the option from case to case of taking other factors into account, including those associated with foreign, industrial, and commercial policy."

[Boxed items]

The Swedish Nuclear Power Inspection Board says no to the export of flash X-ray devices to India, since there is a risk that they may be used for nuclear weapons development:

"Flash X-ray devices are among the so-called "dual-use" products, and find their main application within non-nuclear military research and development. Flash X-ray devices with high voltage, 1,000 kV or more, however, do have a certain significance in the development of nuclear devices.

"India, which in 1974 conducted a test explosion of a nuclear device, has not signed the non-proliferation treaty and has placed only a limited number of its domestic nuclear facilities under international inspection.

"With regard to what was set forth above, and the fact that acceptable assurance has not been given with respect to the non-nuclear use of the equipment and with respect to the documents the Inspection Board otherwise had access to in processing the matter, the Inspection Board cannot support the application."

The products covered in the law on nuclear technology--for example, flash X-ray devices over 500 kV, require export permits because they can be used in nuclear weapons development. The quote is from the Government's bill:

[Text underlined] "Export controls therefore should include only strategically significant products. The requirement that the products shall be strategically significant may then specify that they shall have decisive significance for the production of material for nuclear devices."

Even if the Swedish Nuclear Power Inspection Board, for reasons relating to nuclear weapons, should say no to an export, the government can approve a deal. The quote is from the Government's bill on nuclear technology:

[Underlined text] "Above and beyond considerations of the non-proliferation type, the government naturally has the option from case to case of taking other factors into account, including those associated with foreign, industrial, and commercial policy."

Pakistan

Pakistan is believed to have everything it needs in order to produce nuclear weapons. In the secret facility of Kahuta outside Islamabad, according to American sources, the capability exists of producing about 15 kg of weapon-quality uranium per year.

Pakistan has also been mixed up in several smuggling deals involving nuclear weapons technology, including deals in Holland and the United States. Examples of the products that were halted are high-speed telescopes and ignition mechanisms for nuclear weapons.

In 1984 Swedish authorities stopped the firm of Scandiflash from installing large flash X-ray devices which had previously been delivered to Pakistan.

The primary reason why Pakistan presumably has not yet gone all the way with production of nuclear weapons is pressure from the United States. They have threatened to halt their large deliveries of conventional weapons to Pakistan if the latter becomes a nuclear-weapon power.

India

In 1974 India carried out what Indian sources called a "peaceful nuclear explosion." It is the only test explosion that India has carried out. The official attitude is that they will not procure an arsenal of nuclear weapons, on condition that Pakistan does not.

Rajiv Gandhi, meanwhile, has indicated that India has all the components that are needed to produce nuclear weapons. He has also said that "if we decide to become a nuclear-weapon power, we can do it within a few months at most."

In August India announced that they had dedicated a research reactor that had the capacity to produce plutonium that was not subject to international controls. Despite strong pressure from the United States, India has refused to put several of her nuclear installations under international control, including the facility that produced the plutonium for the test explosion in 1974.

Israel

Israel, which has not signed the non-proliferation treaty, has several nuclear facilities which are not under international control. In some of these it is possible to produce weapon-grade plutonium, albeit in small quantities.

As far as is known, Israel has not carried out any test explosion, but according to international expert opinion, they nonetheless have complete nuclear weapons.

A cautious guess, according to these sources, is that Israel has about 25 nuclear weapons of the Nagasaki size, 20 kilotons.

An American newsletter which is usually well informed in these matters, wrote in May 1985 that Israel had nuclear-tipped short-range missiles of the Jericho II type, as well as nuclear artillery.

Israel has also figured in several illegal deals since the 1960s, when the country got hold of both highly enriched uranium and plutonium.

South Africa

In 1977 American and Soviet reconnaissance satellites discovered that South Africa was building a facility for nuclear weapon tests.

After international pressure, with a threat of breaking off relations with South Africa, they went along with not carrying out any test explosion. South Africa also stated that they would no longer continue to develop nuclear weapons. But they have declined to furnish evidence of this.

In 1979 a U.S. satellite detected a bright flash off South Africa's coast. It was suspected of being a nuclear weapon explosion. No additional evidence for this was made available. According to American sources, however, there is indeed evidence that since mid-1984 South Africa has quietly been increasing her capacity to produce nuclear weapons. According to these sources, South Africa can produce enough highly enriched uranium for several nuclear weapons per year.

United States and Britain Have Tougher Export Regulations

In the United States there are also producers of flash X-ray devices, and in Britain there is a firm that buys Swedish FXDs which are then reexported to other countries. Both in Britain and in the United States, export permits are required for FXDs rated above 500 kV.

FXDs have their own clause in the American export regulations, Paragraph 399.1, item 1553A. This states that an export permit is required for all countries except Canada. The reason for this is given as "national security and the non-proliferation of nuclear weapons."

Other Options

In Britain FXDs are controlled by "Custom and Excise, the Export of Goods (control) order 1985."

But both in Britain and the United States, there are other options besides these regulations which can limit the export even of FXDs with a lower voltage than 500 kV. This in contrast to Sweden, where it is always permissible to export FXDs rated at less than 500 kV.

Small Flash Devices

An example of the tougher regulation in the United States is when an export of "small" flash X-ray devices to Pakistan was halted. It happened when it was revealed that one of the Pakistanis who were to be trained on the FXDs they had ordered turned out to be a nuclear physicist. Such a factor can never halt an export of "small" FXDs from Sweden.

Scandiflash Deputy Director: "I Have No Guarantees"

"Purely theoretically, our largest flash X-ray devices can be used for the development of nuclear weapons. But in practice I think it takes significantly larger machines." So says Arne Mattsson, deputy director of Scandiflash AB, the firm that produces the Swedish flash X-ray devices.

Arne Mattsson also says that he has never seen any connections to any possible nuclear weapon program on the part of the foreign customers which have bought equipment from Scandiflash. "The installations of our machines that I personally studied in Pakistan, for example, also suggest that the application was development of conventional weapons."

No Guarantee

"But I cannot guarantee that none of our machines has become part of a nuclear weapons program; no one can do that," Arne Mattsson believes. "I also tell the FOA what contacts I have had, so that they can check whether there is any nuclear weapons connection with these. But the FOA has never indicated anything in that direction."

Pressure from the United States

The law from 1984 that requires Government permission for the export of large flash X-ray devices is criticized by Arne Mattsson. "I believe it was passed after pressure was applied by the United States. Not because flash X-ray devices could be used for nuclear weapons development, but because for strategic reasons the United States wants to prevent certain countries from reaching too high a technological level."

Unpleasant Monitoring

"We are making a 100 percent effort to eliminate all risks of our flash X-ray devices being used in a nuclear weapons program. But to have to dance to the Americans' piping for other reasons--that I do not care for. I also think it is unpleasant that the Americans are monitoring us in some way that I am not aware of. They are extremely well informed about what we are working on."

Swedish authorities as well are monitoring Scandiflash's doings very closely. "Every time I have come home from a sales trip in Pakistan, for example, I get a telephone call from a Swedish authority that wants to find out what I've been up to," says Arne Mattsson.

/9604
CSO: 5100/2556

VETERINARY PHARMACOLOGICAL, TOXICOLOGICAL DEVELOPMENTS IN HUNGARY

Introductory Identification of Speakers

Budapest MAGYAR ALLATORVOSOK LAPJA in Hungarian No 41 Apr 86 p 197

[Excerpt] The lecture by Professor D. Droumev (Bulgaria) was read by Candidate D. Paskov, docent of the Institute of Pharmacology in the Veterinary Medical Section of the Agricultural Academy in Stara-Zagora with subsequent lectures by Professor M. Kuhnert, head of the Pharmacology, Pharmaceutics and Toxicology Department of the Animal Raising and Veterinary Medical School of Karl Marx University in Leipzig and by Professor E. Werner, head of the Pharmacology and Toxicology Department of the Animal Raising and Veterinary Medical School of Humboldt University in Berlin, and, from Czechoslovakia, by Professor J. Simunek, head of the Pharmacology and Toxicology Department of the Veterinary Medical Academy in Brno and Professor J. Vodrazka, head of the Pharmacology Department of the Veterinary Medical Academy in Kosice.

The lectures are presented in the following, in a slightly abridged form.

State of Drug Supply

Budapest MAGYAR ALLATORVOSOK LAPJA in Hungarian No 41 Apr 86 pp 197-199

[Article by Dr Ferenc Simon]

[Excerpt] With its 6.7 percent share, the manufacture of veterinary products has a prominent place in the Hungarian pharmaceutical industry.

On a global scale, the main groups and shares of veterinary products are as follows:

veterinary products:	45 %
feed supplements:	42 %
vaccines:	13 %

Because of economic considerations, the global trends within the pharmaceutical industry favor an increase in the share of veterinary products. While in the United States, for instance, the cost of developing a human product increased from 12 million to 80 million dollars within the last 10 years and the trial period was stretched from 4 to 9.5 years, the average cost of developing a veterinary product amounts to 20-25 million dollars today and the testing period is 4-7 years.

In the economically advanced countries the view is held that the use of drugs costing up to 5 percent of the total costs of animal raising is remunerative. In Hungary, however, considerably less is spent on veterinary products, about 0.5-0.8 percent of the animal stock values--although this figure is not equal to the previous one, we have no other comparative data--supplemented by the cost of vaccines.

In our country today, there are 90 registered veterinary products supplemented by 25-30 preparations for veterinary use appearing on the imports list. There are 60 premixes containing drugs. In addition, we are also employing 236 so-called FoNoVet preparations for individual use and also about 300 drugs registered for use by humans. Thus, we use a total of about 650 preparations in veterinary practice. This selection is sufficient to treat every disease occurring in domestic animals. The pharmacokinetics of the preparations is also known and thus, by prescribing and adhering to the appropriate waiting periods, we can also guarantee the quality of the food products.

In addition to our preventive programs, primarily through administrative veterinary-hygienic measures, we are also attempting to achieve absence of clinical symptoms by using drugs. Namely, with the use of pharmaceuticals, an absence of clinical symptoms can be achieved rapidly and at low cost thereby reaping considerable economic benefits. In such cases, however, the latent microbiological (subclinical) infection of the stocks is retained. Such diseases are fowl coccidiosis and fowl mycoplasmosis, for example. The achievement of freedom from clinical symptoms by means of medication requires not only drugs but also adequate treatment programs.

Nevertheless, even in Hungary, the majority of drugs is used in a classical manner, for therapeutic and preventive reasons, when the individual diseases appear.

Veterinary-Pharmacological Research

Budapest MAGYAR ALLATORVOSOK LAPJA in Hungarian No 41 Apr 86 pp 199-201

[Article by Dr Drago Droumev]

[Text] During the past 5 years, veterinary-pharmacological research in Bulgaria was primarily directed toward antibiotics and other chemotherapeutic compounds, furthermore, ergotropic, anthelmintic and protozoacidic compounds (including coccidiosis), iron preparations and tranquillizers. According to

the nature of the active ingredient, these studies were of a pharmacokinetic, toxicologic and in part clinico-pharmacological nature with a view on targeted practical demands. The pharmacokinetic work was done using classical methods with a goal of working out their appropriate parameters.

Broxaldin (BA) and broxyquinoline (BH) in a 1:5 ratio is a quinoline-type chemotherapeutic preparation with a broad range of antimicrobial and antifungal effect. By studying its several variations, a preparation by the name of Mastiquin was made for the treatment of mastitis in dairy cows. A recovery rate of 83 percent in cases of mild and 75 percent in cases of acute mastitis was achieved.

They prepared foaming tablets with BA and BH as active ingredients for intrauterine application. They determined that, when a foaming tablet is introduced into the womb, the active ingredients are demonstrable for 24-96 hours and practically none of them enters the blood circulation or milk.

The sulfonamide-trimethoprim combinations were also studied. Detailed studies were conducted on Co-trimedoxine (sulfadoxine + trimethoprim = 5 + 1), trade name Tridoxin, after intramuscular or intravenous injection, on 1 and 2 compartmental models, regarding biological half time, relative distribution volume, total clearance, absorption coefficient, etc., on calves, sheep, piglets and fowl, lactiferous cows and ewes. The waiting time before slaughter is 5 days and it is 2 days with respect to milk; they determmined acute and subchronic toxicity and species-specific tolerance. In the case of acute catarrhous pneumonia of calves caused by Escherichia coli, clinico-pharmacological studies produced an 82-83 percent recovery rate and a 42 percent of recovery rate in chronic processes, with this combination.

They measured the blood concentration of the components, optimal dosage and dosage intervals after the intramuscular administration of Co-trimidine (sulfadimidine + trimethoprim = 5 + 1), trade name Sulfadimetrim, on cows, sheep, pigs and fowl. They examined the distribution of this compound in the organism, its residues in individual organs and in the meat. The cautionary time, that is, the scientifically determined waiting period not prescribed by regulation was determined in fowl.

With respect to 1-phenyl-2,3-dimethyl-4-naphthalanemorpholine-pyrazolinone, the naphthalanemorpholine derivative, it was found that, in addition to its antimicrobial effect, it also has a tranquillizing effect on fowl. Its resorption, distribution in internal organs and some metabolic questions were studied on chickens. Its optimal dosage in the feed was precisely defined.

With therapeutically and prophylactically active antibiotics, some technological conditions were clarified which can be advantageously used in large-scale animal raising (less time consuming, more gentle treatment of the animals) but at the same time provide the necessary prophylactic and therapeutic effect.

An oil suspension was made from gentamicin sulfate which, given intramuscularly in doses of 1.5 mg/kg body mass, provides a therapeutic blood concentration for more than 12 hours. Furthermore, it comes in a water soluble, stable, non-hygroscopic powder form--mixed with vitamins--which can be administered in the drinking water (80 mg/1).The stability of gentamicin foaming tablets in uterine secretion was studied following intrauterine application. The necessary number of treatments was determined. Gentamicin is not excreted in the milk.

From the waste sludge of gentamicin manufacture, an antibiotic complex was isolated--named gentamicin complex II--which differs from the quality specified in the pharmacopoeia and has 40 percent of the total gentamicin activity. It was determined that the acute and subchronic toxicity of gentamicin complex II and its minimal inhibitory concentration (MIC), put in terms of the pure active ingredient, are important in veterinary medicine; tested on 14 different bacterium species, it was not significantly different from the pharmacopoeic
quality of gentamicin. The patients tolerate it well. Administered in the drinking water, the cautionary period was also determined in fowl.

According to clinico-pharmacological studies, good therapeutic results are obtained in cases of coli enteritis of calves (13-21 mg/kg body mass), piglets 12 mg/kg body mass 2 x in 24 hours) and chickens (80 mg/1 of drinking water).

The oily suspension of amoxicillin trihydrate was studied after intramuscular injection of sheep, piglets and chickens. Maximal serum concentration appeared after 2 hours in calves and after 1 hour--depending also on dosage--in piglets, and a bacteriostatic level was maintained for 24-48 hours in ruminants and for 12-24 hours in piglets and fowl. A more precise optimal dosage and period between treatments was provided. The cautionary period before slaughter and the waiting period with respect to milk were determined in cows and ewes.

In sheep infected with Escherichia coli and Corynebacterium, the serum concentration of amoxicillin was found to be twice as high as in non-infected animals. A form of amoxicillin for introduction into the udder of dairy cows was also developed.

Among the Ansamycin antibiotics, work was done on the oily suspension of Rifampicin, called Rifavet. It was shown that, after intramuscular administration, Rifampicin provided a therapeutic level of serum concentration lasting for 12-24 hours in calves, lambs and, depending on the dose, for more than 12 hours in horses and fowl. It is excreted in the milk of dairy cows. But the milk is free of the antibiotic after 48 hours. It was found that Rifampicin has an antiplasmid effect; it is capable of making bacteria belonging to the Enterobacteriaceae group (coli, Salmonella), resistant to antibiotics and sulfonamides on an R-factor basis,--in vivo and in vitro--sensitive again. With respect to drug make up, an intracysternal Rifampicin SV form was selected which stayed within the udder for 28 days.

Experiments were also conducted with polyether-antibiotics.

The nutritive effect of salinomycin-sodium was studied on lambs and animals with ruminal fistula. The dose-dependent beneficial effect on growth and feed utilization (5-24 mg/kg feed) was confirmed; the positive effect on the growth of wool, the molar increase in propionic acid in the rumen and a simultaneous decrease in the butyric acid, valeric acid and acetic acid concentrations could be demonstrated. There was an increased alkali reserve and blood sugar level and a decrease in the amount of urea and ketone bodies, and a modest decrease in the infusorium count coupled with qualitative changes. Salinomycin (75 mg/kg feed) eliminates the resistance (antibiotic, sulfonamide and nitrofurane resistance) of coli bacteria. Using lasalocid-Na, it was determined in calves that a nutritive effect analogous to salinomycin can be brought about only by relatively larger doses and the effective ergotropic dose was also much higher in lambs (50-60 mg/kg feed). Lasalocid does not eliminate the R-factor resistance to drugs in cases of bacterial infection in chickens.

The results of preclinical, and furthermore, of clinico-pharmacological and field tests with monensin-sodium in the Bulgarian People's Republic provided similar anticoccidial and toxicity data as with the foreign preparation. Turkey chicks, geese and ducks show an increased sensitivity to it.

Studies were conducted with nutritive antibiotics. Thus, with respect to toxicity and nutritive activity, there is no essential difference between the domestic Flavophospholipol (Flavorpharm-VRb) and the original one from abroad. It raises the Grill-value and the ratio of internal organs--compared to the bones. It was found that it brings about an increase in the amount of protein, the DNA/RNA coefficient, the fat content of the meat, furthermore, the cyanocobalamin and ubiquinone levels. In fattening geese, it has a dose-dependent nutritive effect with special emphasis on its property affecting the liver and its quality. Residual antibiotics were not found in the meat and internal organs of either the chickens or the geese.

Thanks to its R-factor antiplasmid effect, its effect on eliminating the antibiotic and combined sulfonamide + nitrofuran resistance of coli bacteria was noted both in vivo and in vitro. In lambs with a developed rumen, flavophospholipol has a nutritive effect.

The zinc-bacitracin (Bacipharmin) also has a nutritive effect on fattening geese similar to flavophospholipol including an increase in body mass and improved liver quality.

It eliminates the R-factor resistance of coli bacteria against antibiotics and combined sulfonamides + nitrofurans.

Our experiments with interferon-inducing compounds suggest that Dipiridamol is a very promising preparation in chickens at doses of 27 mg/kg body mass, administered 2 x in 2 days. In the 24th and 48th hours, it provides a high interferon titer which is still retained at a lower level until day 7, simultaneously raising the lysozyme content and phagocyte activity.

Detailed studies were conducted with an iron-dextran complex (Dextofer 100). This compound has an antiallergic and antiexudative, H^[U1^[D-receptor inhibitory, antiserotonin, alpha-adrenolytic, myorelaxant and mildly ionotropic effect. Dextrofer 100 protects against anemia developing in twin calves, furthermore, 2-7 day old calves born during the winter or early spring months and newborn lambs weaned after 3-5 days; it heals when necessary, and it discolors the tissues at the injection site only briefly (for about 10 days) and not excessively.

Antiprotozoal compounds (except coccidiostatics) were not intensively studied in the Bulgarian People's Republic.

An interesting finding is that silymarin (from Silybum marianum) has a protective effect on the liver; administered orally in a 3 percent solution, twice daily in 60 ml doses for 10-12 days, it has a therapeutic effect on the fatty liver dystrophy of high yielding dairy cows.

It is evident from the report that, in the field of veterinary pharmacology, studies of both scientific and practical significance were conducted during the past 3 years.

In addition to the antibiotic and chemotherapeutic compounds, which have a central place in the pharmacological laboratories, research is prominent with respect to solving the inhibition of the development and elimination of R-plasmid resistance. Thereby lifespan is extended, the indirect effectiveness of the applied antibiotics is increased and the immune protection of the animal organism is enhanced--by way of drug administration. We shall continue work in this direction in the coming years. But we also want to study intensively those rational therapeutic possibilities which correct the non-favorable pharmacokinetic parameters of individual drugs, optimize them and thereby become very useful in the prophylactic and therapeutic care of the animals.

Future Integration in Biotechnology

Budapest MAGYAR ALLATORVOSOK LAPJA in Hungarian No 41 Apr 86 pp 201-203

[Article by Dr Manfred Kuhnert, GDR]

[Text] Pharmacological Studies in the GDR

Our main research topics can be grouped as follows:

Specific veterinary basic research (with particular emphasis on the prevention and treatment of enzootic diseases appearing under conditions of industrial, large-scale production).

Development of test models for examining new chemical compounds (in vitro, animal experiments, mathematical models).

Development and field testing of preparations (medications, disinfectants, vaccines and diagnostic preparations).

Quality control of active ingredients and preparations.

The work to accomplish the tasks listed is distributed among four veterinary pharmacological and toxicological institutes. Basic pharmacological research is conducted primarily at Humboldt University where the active ingredients of medications and of disinfectants are also studied. In contrast, studies carried out at the Pharmacological, Pharmaceutical and Toxicological Institute of the University of Leipzig have a mainly toxicological profile. However, future work at the institute is becoming increasingly integrated with the central biotechnological research program and, within its framework, active ingredient and immunotechnical studies are coming to the forefront. On the other hand, future clinicopharmacological and toxicological studies for the chemical, feed and pharmaceutical industries will be conducted mainly in the Central Institute of Veterinary Pharmacology and Toxicology established in 985.

All research and development (R&D) work is centrally coordinated by the State Animal Health Institute in Berlin. Especially noteworthy here are the supervision of clinical studies involving new veterinary medicines and vaccines, toxicological control of active agents permitted in the feed and the study of residual contamination in foodstuffs of animal origin.

The main trends of veterinary pharmacological research are summarized as follows:

In the field application of antibiotics, a joint human and veterinary medical strategy must be developed. In addition to antibiotics, an important alternative possibility is offered by the use of substitutional agents (natural products such as humic acid, pentonites, etc.) in certain areas of indications.

In the regulation of reproductive biological processes and commercial animal husbandry, synchronizing compounds and preparations influencing readiness for conception are the most important ones.

The development of immunoprophylactics and widening the choice of diagnostic preparations are also important research areas. For instance, the development of vaccines which could be orally administered to fish (especially in fresh water fisheries) are of economic importance. The development of new disinfectants suitable for local and external treatment also presents a constant research task in the interest of decreasing resistance and eliminating side effects.

More Important Problems of the Biotechnological Integration of Pharmacology and Toxicology

Basic Principles

The new tool of biotechnology consists of the cell-substrate-bioreactor system where the microorganisms, the animal and plant cells and the enzymes function as a new production tool. There are enzymes, the biocatalysts, which increase the rate of chemical reactions within the cells by orders of magnitude of 100 million to 10 trillion (10^[D8^[U-10^[D13^[U) and, under suitable conditions, produce very extensive cell growth in the technical systems. A single bacterial cell could produce 35 trillion progenies within 24 hours. During the same period, under suitable conditions, 500 kg yeast could produce 50 tons of protein. In contrast, a 500 kg cattle produces only 500 g of protein during the same period.

The supply of protein, of great value in human nutrition, is a general problem and, therefore, during the past few years attention has again been focussed on procedures aimed at producing microbiological proteins. By selecting the appropriate microorganisms and substituting the missing components (for example, methionine), the animal feed produced in this manner attains optimal nutritional value. The direct use of such microbiological proteins for human nutrition must also be considered in the future. In the course of this process it is important that the microorganisms are also capable of obtaining the energy needed for their growth and for their components from non-traditional sources. Certain yeasts can also utilize crude oil, there are methane and methanol converting bacteria and protein of high value is formed as a result of their activity. These possibilities are already utilized in the Soviet Union, England and the GDR and they far surpass the processes customarily used earlier by the pharmaceutical industry.

A special product, named Fermosin, was also produced in the GDR. It will provide savings on protein imports (soy, fish meal) of considerable importance for the economy of the GDR.

The Advantages of Biotechnology

The industrial utilization of biotechnology is increasing at a rate much faster than average. The use of antibiotics, new feed components and feed supplement preparations as well as of bacterial fertilizers and plant protective compounds provide the basis of our nutrition. The biotechnological procedures of today also contribute to keeping the air and waters clean.

Current State of Biotechnological Development in the Capitalist Countries

In the United States, at the cost of enormous investments, an attempt is being made to utilize consistently the possibilities of biotechnology; essentially similar efforts are made also in the other capitalist countries. The Japanese look upon biotechnology as the last great technological revolution of our century. Next to the United States, Japan has the best possibilities for financially supporting biotechnological research. Biotechnology was assigned national priority by the Japanese government and it is supporting such development. In 1981, a 10 year program was launched for developing industrial biotechnology the main trends of which include the development of bioreactors, gene technology and industrial cell cultures. The GDR is also increasingly encouraged in this direction by its strong chemical industry and the given traditional experiences in the field of biotechnology.

Large-Scale Production of Monoclonal Antibodies

As soon as monoclonal antibodies will be marketed, they will belong among the most important biotechnological products. They will be used in diagnosis, therapy and also in the selective purification of active agents. Their importance is steadily increasing.

For instance, Hoffmann-La-Roche alone uses kg amounts of them for interferon purification. Using certain procedures, other living cells can also be processed such as, for instance, recombinant bacteria or insulin producing pancreas cells. Within the framework of an agreement with the National Cancer Institute, there are many who also want to study monoclonal antibodies in cancer therapy.

At the same time, the BIO-Response company (California) is employing a completely different procedure. In their method called Mass Culturing Technique, they use cattle lymphatic fluid, purifying it by means of a suitable filtering system from every cell and material which could inhibit the growth of hybrid cells or could contaminate the monoclonal antibodies. Because of lack of space further description of the method is impossible.

DNA-Probes: By-Products of Monoclonal Antibodies

According to a report by Biomedical Business International (BBI), the DNA-probes can be used for studies involving infectious diseases, cancer diagnosis, drug sensitivity, tissue typing and a list of veterinary and agricultural studies. According to the BBI report, some of the DNA-probes (small DNA segments serving as a substitution of part of the natural DNA) are already available for virus diagnostics and some of them have already been marketed.

Biotechnology in the Soviet Union

In its resolution of June 1981, the Council of Ministers of the Soviet Union designated further basic research, carried out in the area of physicochemical processes of life, as one of the most important problems of current Soviet science. This means the provision of more favorable conditions for rapid advancement in the biological sciences and broader application of the results in agriculture, medical science and industry. To achieve it, a national biotechnological program was set up and, to guide it, the State Biotechnological Council was established which coordinates the work of every participant and, in the course of it, establishes the priorities.

In the Soviet Union, as in the other industrially developed countries, the use of gene technology in the field of active agent production is in progress on a vast scale. Microorganisms suitable for the production of interferons, insulin, proinsulin, human growth hormone, ovalbumin and other proteins were developed by Soviet scientists.

Final Conclusions Concerning the Possibilities of Applying and Utilizing Biotechnology in Animal Raising and Veterinary Medicine

Within the framework of research conducted at the institutes of highest learning in the GDR, the biotechnological research and development activities are planned to be establised at the universities of Halle and Leipzig. According to this plan, the Animal Raising and Veterinary Medical Section of Karl Marx University in Leipzig will join two basic projects. One project involves basic cell technological research in the field of reproduction biology. The other main project is concerned with active agent and immunotechnical research. The latter project also includes the fields of pharmacology and toxicology. In this project, the active agent and immunotechnical studies will be conducted in three steps, according to the plans.

1. Basic research to develop procedures for the biological-biochemical synthesis of homologous bioactive materials. This encompasses basically two versions. One possibility is to produce and develop active ingredients based on the recognition of the physiological characteristics of the living matter (cell, isolated organs, the whole organism). The other modification is in vitro total synthesis after elucidation of the physiological characteristics of the new compounds. Both possibilities must be considered and both modifications must be developed so that, within a short time, results of practical utility could be achieved with them.

2. Studying the properties of active agents produced in step 1 and using them as models for practical application.

3. Preparing for and organizing the industrial production of the active agents.

Because of the composition of the Animal Raising and Veterinary Medical Section of Karl Marx University in Leipzig the simultaneous presence of representatives of many branches of science provides favorable possibilities for integration and for the interdisciplinary development of the following research areas:

production and study of the specific active agents influencing growth and production processes;

isolation and development of natural and synthetic immunomodulators for active and passive immunization against infectious animal diseases;

isolation and development of active materials acting as bioindicators for purposes of veterinary diagnosis and kinetic studies conducted on warm blooded animals;

isolation, production and further development of medications, plant protecting preparations and other bioactive compounds;

research on and production of cell-specific active agents for the regulation and enhancement of reproductive biological performance;

development of active materials (microbiological factors, amino acids, proteins) for enhancing the improvement and more effective utilization of feeds as well as the nutritional physiological capabilities of domestic animals.

The basic requisite for realizing the goals listed is, on short order, a material-technical base, especially the provision of suitable technical equipment in the laboratories. The beginning of experimental work is planned for the next Five-Year-Plan period. Realization of the tasks mentioned will represent a considerable change in the profile of pharmacology and toxicology compared with the content and methodology of current research and it will place very high scientific requirements on workers in this area of science.

Toxicological Problems in Testing Active Agents

Budapest MAGYAR ALLATORVOSOK LAPJA in Hungarian No 41 Apr 86 pp 203-205

[Article by Dr Eberhard Werner]

[Text] During the past 5-10 years, several singificant toxicological problems with a bearing on animal health were solved in the GDR. The studies were conducted at the animal health and agricultural institutes. Let me present some examples.

When nitrite-nitrate feed is used, it is important to study the state of health and metabolism of the animals, above all in cattle raising which plays a big role in our animal production. In this respect the primary studies involved the interaction between nitrogen containing compounds and essential components, trace elements and vitamins. At the same time, other questions were answered such as, for instance, the influence of impurities, the effects of certain storage conditions, chemical fertilizers and harvest timing on changes in the nitrate content of feeds. Based on the results, new agricultural and animal health regulations were issued.

Recognition of the direct and indirect effects of environmental pollutants on various animal species represented an additional research area. Most of all, it involved elucidation of the role of mercury, lead, cadmium, sulfur dioxide and cyanides. These studies were conducted not only on domestic commercial animals, bees and fishes among them, but also on wild species, deer, wild pigs and pheasants. The studies had a very broad spectrum. The main goals were: evaluation and teratological testing of organ-specific residual compounds, refining of analytical methods, examination of the relationship between environmental pollution influencing the state of health of the animals and the quality of feed, and the exploration of the regional expansion of industrial activity.

As additional complex work, let me mention the toxicological evaluation system of pharmaceutical research which is conducted as in every other country. In this area, I will only mention the studies still in progress involving materials with a lasting effect which have been conducted in the course of ovulation synchronization and induction studies, furthermore, the series of

broad observations associated with natural materials and their more important refined derivatives. With respect to the first problem, the studies have not yet been completed while in the second series of complex problems, for instance, the studies elucidating the toxicity of luminic acid as a function of various modes of administration provided very interesting data especially with respect to further utilization of the compound. Publications by Bentz, Kuhnert and Golbs refer to it unequivocally.

But other significant normal toxicological problems could also be mentioned such as testing the innocuity of new construction and auxiliary materials used in agriculture, evaluating feeds prepared through biotechnology, testing rodenticides, insecticides and disinfectants, evaluating materials with an ergotropic action and many other topics. In our country, just as in other countries, the above mentioned problems are in the realm of veterinary toxicology.

At this time, only two problems will be discussed in more detail which--in my view--are of general interest and are given increasing attention in the toxicological research of the country. I want to make some remarks on the evaluation of toxicological studies related to the circadian rhythm (daily rhythmic changes within physiological limits) of experimental animals and on the problem of the immunosuppressive effect.

In the course of toxicologial testing, the effect of active agents on the immune system of animals is judged and evaluated to varying degrees in the international literature. There is complete agreement among scientists in that these tests need to be performed if the active agents exert a direct effect within the animal or human organism for a prolonged time. Ergotropic compounds, feed components produced by biotechnology and drugs regulating parturition are among this type of compounds. On the other hand, in immune system comparisons, views differ with respect to the individual animal species and the species of experimental animals used as models, and also with respect to the suitability and sensitivity of the test methods.

In various broad range experiments for evaluating the immunogenic effect of feed components and ergotropic compounds, the following procedures were employed.

Non-Specific Resistance:

white cell count, differential count, granulocyte-lymphocyte ratio;

in vitro tests using P^[D32^[U-labelled brucellae measuring the radioactivity of granulocytes;

lymphocyte transformation test which was performed using phytohemagglutinin as the non-specific stimulator compound, measuring the radioactivity of tritiated thymidine (T-lymphocyte function test);

determination of the serum immunoglobulin (IgM and IgG) content by means of the electrophoretic immune diffusion technique;

determination of the mass of certain organs such as, for instance, the spleen, thymus and, in fowl, the bursa Fabricii, and their ratio to the body mass of the animals;

histological examination of the above tissues.

Specific Immunity:

Immunization with bacteria, for example brucellae, viruses, such as the Aujeszky's virus, and with heterologous proteins, such as sheep erythrocytes, and a subsequent study of antibody dynamics or the serum neutralization method;

study of allergic reactions such as, for example, the tuberculin test, after previous sensitization with killed antigens.

The appropriateness of the test procedures was compared with positive control groups. The control animals were treated with known immunosuppressive materials, for example cyclophosphamide or an organic compound containing tin (dioctyl-tin-oxide). The studies led to the conclusion that a homogeneous group of experimental animals, preferably SPF-individuals, are definitely needed for such work. The studies must be carried out on the animal species which is slated to be treated with the particular material.

It is rather difficult to distinguish between the individual methods. It can be concluded, however, that the simple labor-technological methods such as, for instance, evaluation of the leukocyte count, that is, a change in the granulocyte-lymphocyte ratio or, in the hemolysin test performed after immunization with heterologous mammalian protein, the determination of hemolytic antibodies as a function of the complement or, the checking of allergic skin reactions as well as the mass ratio of the bursa Fabricii of fowl, can be valuable indicators for evaluating the immunomodulator effect. However, comparison of the results of various test methods, performed simultaneously, is absolutely necessary. In past years, similarly to immunological problems, the biorhythmic processes of animals were frequently analyzed in the international literature; especially with respect to the behavior of the experimental animals, the differences found among the individual animal species with respect to pharmaceutical research, sleep-wakefulness, feed intake and some other problems. During the past years, in some of our initial experiments, our group studied the influence of the circadian rhythm on physiological parameters such as body temperature and motility of the experimental animals and the toxicological characteristics of compounds, for instance, changes in supersensitivity or the LD^[U50^[D-value.

In the literature, data on the varying sensitivity of the animal or human organism as a function of the daily rhythm were registered from various angles. Symptoms of certain diseases, such as bronchial and cardial asthma in humans, usually appear during the hours shortly before midnight. There are poisons, drugs, bacterial endotoxins and carcinogenic compounds which produce significantly different effects depending on the time of administration. Consequently, for instance with respect to medications, identical therapeutic effect does not develop any time of the day, even in the presence of identical

blood concentrations. These differences depending on the time of the day are important especially during toxicity studies. For instance, 190 mg/kg body mass of phenobarbital given to rats at 1 pm is a 100 percent lethal amount while the same dose given between 11 pm and 2 am is survived by every animal.

In setting up the protocol for studying the circadian rhythm, the 24 hour fluctuations in body temperature were also evaluated. On this basis two materials were studied which influence the changes in body temperature through different action mechanisms:

sodium nucleinate, as a standard pyrogenic compound used in several countries, can also be used in non-specific stimulus therapy;

dinitroorthocresol (DNOC), one of the herbicide and insecticide compounds.

White male mice were used as experimental animals. They were kept in a 12-12 hour day-night rhythm. The days were set between 6am and 6pm. The accommodation period lasted at least 28 days. In the sensitivity test, administration of a median lethal dose, that is, 2165 mg/kg body mass, started at 6 am and continued at 4 hour intervals, revealed that the percent mortality was highest at 2am (76.7%) and at 2pm (63.3%) while the lowest level of losses was recorded at 6am (20%) and 10pm (46.7%). The data show that sodium nucleinate is more toxic during the rest period of the animals. These times coincide with the lower locomotor activity of mice and the lower ATP content of liver cell mitochondria.

Studies conducted under a similar experimental protocol revealed that the LD^[U50^[D-value of DNOC is also a function of the time of administration. Administration was started at 4am at 4 hour intervals. The most pronounced toxic effect was observed at 8pm, after administering 24.53 mg/kg body mass DNOC while at 12 noon, the LD^[U50^[D value was 28.08 mg/kg body mass. Consequently, the greater sensitivity of the mice was at the beginning of the activity phase.

In general, on the basis of the chronotoxicological studies, it can be stated that they are indispensable for the toxicological characterization of individual compounds; in addition to naming the animal species, the time of the studies must also be reported because there are very divergent differences among the animal species with respect to the active and resting phase of their metabolism.

Chemotherapeutic-Compounds, Drug Interaction Experience

Budapest MAGYAR ALLATORVOSOK LAPJA in Hungarian No 41 Apr 86 pp 205-206

[Article by Dr Jan Simunek, CSSR]

[Text] The therapy of infectious and parasitic diseases of animals is steadily in the center of attention and, in view of the industrial scale conditions of raising domestic animals, veterinary practice also poses great demands on this field.

The Czechoslovakian experience with the subject under discussion shows that if 1 year was needed to introduce a new medication in practice in the past and 2-3 years still appeared sufficient to amass the necessary information in 1960, this period can already be designated as 7-10 years since the 1970's. Because of stricter control studies and numerous other requirements, there has been a considerable decrease in the number of new drugs and, in turn, the cost of their development has increased almost excessively (on the average 10-20 million GDR marks) which by now can only be covered by enterprises well provided with capital. Ten years ago, the number of these new drugs was estimated as between 20-50 on a global scale.

During the past 5 years, our biggest enterprise manufacturing veterinary products (Spofa) released a few new drugs for general practice. Organization of their domestic production decreased the demand for imports and it also made possible a considerable modernization of previous formulas of well-known drugs used in general practice. As an example, the thorough and broad testing of a quinoxaline derivative resulted in the marketing of a new preparation under the name Cyadox.

It is important to stress that, during the past period, chemotherapy was not the most important trend among the activities of Spofa in the research and development of veterinary products. The activities were mainly in the area of regulating physiological functions (reproduction of the animals and pharmacostimulation of their yield) where significant successes were achieved.

In the development of antimicrobial and antiparasitic materials, the following results were achieved:

an independently developed technology for monenzin production; a domestic method for tylosin production; development of a tylosin preparation into Vubityl injection and the orally administered Vubivet; the Oraclen foam for the treatment of chronic mastitis; changing the packaging form of Oxymykoin (oxytetracycline) for practical reasons.

Additional important results: the production of Coryphamin (diamphenetide), a flukicide; innovation of the active agent and packaging of Helmirazin, an anthelmintic; development of a Helmisan premix preparation for useful wild animals; combination of the Rafoxanide-Mebenvet premix for hoofed wild animals; the study of Sulfakombin, an anticoccidial preparation; a potentiated sulfonamide preparation, Duon foam, for the treatment of mastitis; production of a uterine rod combined with sulfonamide for the treatment of complications caused by a retained placenta.

We also solved the domestic production of the already mentioned quinoxaline derivative, Cyadox, accomplishing the study of the antibacterial effect and the growth stimulating properties of the compound and also its toxicology; as new preparations, we evaluated the Vubiadox T (with tylosin) and Vubiadox F (with phthalyl-sulfonamide-thiazole) combinations.

The list of names reveals that we are paying adequate attention to the field of chemotherapy both in terms of research and development but, with respect to truly new results, the situation is difficult also in our country and thus it is natural that practical needs in the area of chemotherapeutic compounds are often satisfied by imports.

Several years ago, we defined the trend for the research activities in our department; we strongly considered the fact that Spofa's research base is so large that cooperation with clinical-type research establishments for the development of new preparations becomes superfluous. Thus, our activities are directed toward the study of basic research-type problems. However, the topics are selected with a view to possible practical applications which can be exploited as veterinary preparations, including those manufactured by Spofa.

During the past 5 years, many experiments were conducted with sulfonamides. Above all, interactions with other materials were studied, especially those ingested for longer periods by our domestic animals under industrial conditions in the form of medicated feed or those which got into their organism as a result of chemical processing. For instance, the manifestation of interactions was studied between products contributing to the increase in the animals' body mass and vitamins, antibiotics or tranquilizing compounds, furthermore, evaluations were made of the same effects between anticoagulant rodenticides and vitamin K. On the basis of our experiments, the following conclusions can be drawn:

1. Use of the A-, C- and B-vitamin complex has no effect on the kinetics of intramuscularly administered sulfamidine in domestic rabbits.

2. Brodifakum and vitamin K^[U3^[D influence the kinetics of sulfonamides.

3. When administered to chickens orally or in injection form, the blood concentration of sulfadimidine was not changed by monensin, lasalocid and salinomycin.

4. The concentration of orally administered sulfadimidine in the blood of chickens and in the small intestinal (jejunal) content was not altered by feed containing monensin or lasalocid.

5. The use of phenobarbital in chickens has no effect on their blood sulfonamide concentration.

6. Sulfonamides increase the stupor of chickens caused by phenobarbital.

7. Sulfadimidine influences the acute toxicity of phenobarbital depending on the time interval between the use of the two compounds and also on the age of chickens or mice.

8. The simultaneous administration of sulfonamides and diazepam--among others-changes the blood concentration of sulfonamides. This change is influenced by the species and sex of the animals.

9. Interaction was also demonstrated as a result of oral use of sulfonamides and Cyadox therapy, manifested by a decrease in the blood sulfonamide concentration in mice and older chickens. A decrease in blood concentration did not occur when the sulfonamide was injected.

New Organotropic Preparations

Budapest MAGYAR ALLATORVOSOK LAPJA in Hungarian No 41 Apr 86 pp 206-207

[Article by Dr Josef Vodrazka, CSSR]

[Text] Permit me to report on the results of pharmaceutical research in Czechoslovakia--with no attempt at completeness--in the following.

A) Preparations Affecting Reproduction

In recent years, several new preparations have been marketed for the treatment of reproductive disturbances and for the targeted regulation of the physiological processes of reproductive organs. These medications are utilized in medical but even more in medical-biotechnical areas.

1. The domestic, original synthesis of Cloprostenol was worked out. Thus we are among the few countries where this important hormone has been produced for a few years by now. It is marketed in sufficient amounts not only to satisfy domestic needs but also for export to socialist and other countries.

Cloprostenol is the analogue of PGF^[U2alpha^[D. In Czechoslovakia, it is available under the name Oestrophan. Each ampoule contains 500 micrograms of active agent in the form of its sodium salt. The effects of this luteolytic compound are probably explained in terms of its narrowing of the uterovaginal arteries whereby the cells of the corpus luteum do not get nourishment. However, it is also possible that the prostaglandins interfere with the synthesis of progesterone. It is an interesting observation that their effect is negatively influenced by antiinflammatory compounds.

With respect to the medical-biotechnical use of PGF^[U2alpha^[D the most important area of its application is the synchronization of ovulation in cattle. The 500 microgram dose must be injected into muscle twice: the first injection is between days 40-60 after calving irrespective of the cycle. The second injection follows 11 days after the first. The animals are inseminated 72-76 hours later and they are reinseminated a day after that.

In the presence of functional disturbances involving the ovaries, anestrus, endometritis or pyometra, 1000 microgram is injected. Insemination is carried out during the first estrus. Should an estrus fail to develop, the first dose is followed by injection of another dose 11 days later. The animals are inseminated 72-76 hours after that.

In the case of a follicular cyst, 1000 microgram cloprostenol is administered 10 days after the choriogonadotropic hormone preparation (this can be Praedyn inj. or Praedyn comp., the latter containing HCG + progesterone). At times the cloprostenol + gonadorelin combination (Dirigestran inj.) can also be effective.

Endometritis is treated with 1000 microgram cloprostenol in combination with intrauterine therapy.

The studies involving induction of calving in cattle are not yet completed. In sows the compound can be used between the 111-113th day of pregnancy. Farrowing occurs within 25-40 hours.

The withdrawal period after the use of cloprostenol was recently set--internationally--as 2 days for meat and 24 hours for milk. In some countries, however, its use in dairy cows is not permitted.

A similar preparation among the list of prostaglandins is Alestrum inj. containing 125 microgram fluprostenol in 1 ml solution, also in the form of its Na salt. The preparation is recommended for mares. The indications are: functional causes or anestrus associated with lactation (silent estrus), long diestrus, corpus luteum persistence and chronic endometritis. Undesired pregnancy can be resolved by precipitating abortion. The preparation causes hyperhidrosis lasting about 1 hour. Its use is contraindicated in the presence of digestive or respiratory disorders.

2. In addition to the former, decapeptide GnRH, gonadotrope-realizing hormone was also synthesized as gonadorelin. The commercial preparation is named Dirigestran inj., containing 40 micrograms of active agent in 1 ml of solution. Following its injection, an increased LH (luteotropic hormone) level in the peripheral blood persists for 30-180 minutes. In cows, especially in cases of anestrus associated with cystic ovarian degeneration, it is indicated alone or in combination with HCG or progesterone. Another possible use is in the treatment of irregular ovulation. Its intramuscular dose is 100-250 microgram. Larger doses are recommended in cases of persistence of the disorder. The therapy can be repeated if necessary, sometimes combined with cloprostenol.

3. The karb-analogue of Oxytocin, karbetocin by its international generic name, was produced by an original (Czech) synthesis. The commercial preparation is named Depotocin inj. and it has 0.2 mg (10 IU) active agent in 1 ml of solution. A favorable property is its prolonged effect because the compound metabolizes slowly. Indications are: prolonged parturition, retention of the placenta, evacuation of pathological secretion from the womb, acute and chronic post partum endometritis, induction of the lactation reflex in heifers and cows. In biotechnical usage, the puerperium of cows and sows can be shortened in a targeted manner with karbetocin. Dosages are largely identical with oxytocin.

4. From among the older preparations, Agelin with a metenchlormadinone base proved to be effective in synchronizing the ovulation of sheep. The tampons must be placed into the vagina 14-17 days before the planned insemination and they must be left there for 12 days. After their removal, 500 IU PMS should be injected into muscle.

5. A metallibur derivative from the list of carbamoylhydrazines, named Evertas P, is available for synchronizing the ovulation of sows. In 1000 g of medicated feed there is 5 g zinc-metallibur. The medicated feed mixture should e fed for 20 days. Estrus appears 5-8 days after the end of treatment.

6. In many cities of our country, pidgeon overpopulation is a serious problem. The granulated preparation, Malotin, contains 4 g busulphan in 1000 g of carrier. Good results were obtained under experimental conditions. Busulphan suppresses both spermiogenesis and ovogenesis. The number of eggs is decreased and many of them are sterile. Thereby the number of pidgeons in a city can be reduced by one-third and even more. However, busulphan is an antitumor drug and, consequently, permission for its widespread use is currently under consideration by health officials.

B) Other Preparations

In Czechoslovakia, several preparations with a depressant effect are available built on an ataractic, neuroleptic and sedative base. These are used for medical and medical-biotechnical purposes.

The Diazepam Spofa premix for veterinary use contains 30 mg active agent in its 1 g unit. In addition to its tranquilizing effect dissolving nervous systemic tension, this ataractic also has muscle relaxant and antispasmodic properties. It reduces the aggressivity and restlessness of animals especially in the course of regrouping. The effects begin in about 30 minutes and last for 4-6 hours. Adaptation of the animals is promoted by the preparation; it can be used to facilitate transport or other kinds of handling of the animals. It must be mixed with feed. Diazepam Spofa suspension can be employed for individual use. The waiting time with both preparations is 72 hours for meat and 24 hours for milk.

Chlorprotixen-methanesulfonate is the active ingredient in two preparations: Sedonal inj. contains 130 mg/ml of solution. As a tranquilizer, it is injected into a muscle or vein before examination or other medical procedure. It cannot be used in animals transported for slaughter. It is very useful, however, as premedication before anaesthesia. Sedonal pulv. contains 20 g active ingredient in 100 g carrier. It should be used mixed in the feed. Duration of the effect is 3-4 hours for both preparations. Waiting time in general is 3 days, 5 days for meat. Sedonal pulvis cannot be given to dairy cows.

Sedophen pulv. Feed premix; In 100 g of carrier, 4 g with phenobarbital. As a sedative, it can be used in large-scale fowl raising, mixed with the feed, over 3-5 days. Waiting time is 7 days for meat.

Rometar 2% inj. is marketed with 20 mg/ml xylazine as active agent. It is widely known that, in addition to its sedative effect, the preparation is also an analgesic. It must be injected into muscle or slowly into a vein. In some cases it is combined with a local anaesthetic. Waiting period is 2 days for meat, 7 days for kidney and liver.

A preparation containing amino acids was recently marketed under the name Heperemin inj. In 1 ml of solution, it has 100 mg l-lysine and 25 ml d,l-methionine. Indications are: deficiency in these amino acids, disturbances in the acid-base equilibrium, liver degeneration and other liver disorders. It can be effectively used in treating immunodeficient, weakened young animals, myoglobulinuria of horses and certain types of poisoning. In these cases, and also in the presence of liver disorders, it must be administered with glucose. Studies conducted under a similar experimental protocol revealed that the LD^[U50^[D-value of DNOC is also a function of the time of administration. Administration was started at 4am at 4 hour intervals. The most pronounced toxic effect was observed at 8pm, after administering 24.53 mg/kg body mass DNOC while at 12 noon, the LD^[U50^[D value was 28.08 mg/kg body mass. Consequently, the greater sensitivity of the mice was at the beginning of the activity phase.

In general, on the basis of the chronotoxicological studies, it can be stated that they are indispensable for the toxicological characterization of individual compounds; in addition to naming the animal species, the time of the studies must also be reported because there are very divergent differences among the animal species with respect to the active and resting phase of their metabolism.

2473
CSO: 2502/57

POLISH RAILROADS INSUFFICIENTLY AUTOMATED

Warsaw PRZEGLAD TECHNICZNY in Polish No 7, 16 Feb 86 pp 12-13

[Interview with Andrzej Maciejewski, MSc (Eng), assistant director of the Institute of Automatics and Telecommunication of the Main Railroad Engineering Research and Development Center, transcribed in a narrative form by Wojciech Adam Pawlowski: "Modern Control Technology"; date and place not specified; the first paragraph is an editorial introduction]

[Text] Railroads in Poland do not enjoy the best of reputations. This should not be surprising, because in the mind of the average citizen they are generally associated with the notion of an obsolete means of transportation carrying passengers and goods too slowly and in poor conditions. There is a view that one of the reasons for this situation on the railroads is their technological backwardness. Automation and electronization are offering an important opportunity for progress. What place are they going to have in railroads, and what is going to be done for them to be able to achieve more than they have until now, especially in controlling railroad traffic? The subject is discussed below by Andrzej Maciejewski, MSc (Eng), assistant director of the Institute of Automatics and Telecommunication of the Main Railroad Engineering Research and Development Center.

The level of automation and mechanization in railroad transport is insufficient, which has negative consequences for the general maintenance of the railroads, the regularity of traffic and the working conditions at PKP [Polish State Railroads]. The factors determining the introduction of innovative technology should be economic effects, the level of safety achieved and regularity of traffic. Until now, automation has been introduced in railroad transport on a large scale only in bookkeeping, statistics and office documentation. It is also being introduced into other areas, including at sorting yards, with troubleshooting, etc. This has been conducive to increasing the traffic capacity of the stations, faster turnover of rolling stock and locomotives, higher terminal capacity and the resulting reduction of spending on new construction. It also reduces the need for hiring more employees, something that is becoming increasingly more difficult.

The elements of automatic control systems are installations at stations and on the lines, systems of automatic train braking, remote control and traffic control, automatic crossing signalization and automation of sorting yards.

Currently, various types of station facilities are being used. The majority are obsolete mechanical or electromechanical (about 75 percent) switches that are 70 years old or older. The maintenance of this equipment requires extensive efforts by operation services. Only some 25 percent of traffic control equipment can be automated. These are various types of relay devices. They make it possible to reduce the number of switch circuits and thus reduce the number of service employees while at the same time enhancing the safety of railroad traffic and the traffic capacity of the stations. In the 1970's a license was purchased for a modular geographic system of station control facilities (from the firm Ericsson), but this system failed to meet expectations. The reason was that the core element of the system--the so-called small-sized JFR relay--failed to meet the operation safety requirements at subsidiary stations. In the next few years there are plans to introduce microprocessor systems at station control facilities, which will allow expanding the functions of the basic equipment and traffic control systems.

Most common on the tracks are semiautomatic blockage devices. About 15,000 km of lines are equipped with them. They do not, however, control so-called occupied tracks; the safety of traffic depends on people working at stations and road posts. And all kinds of things can happen to them. Semiautomatic blocking (with electromechanical relay or LPB blocks) cannot be used on tracks with automatic traffic control. Old semiautomatic blocking equipment has to be replaced by units that can monitor the occupation of the tracks between stations (electronic interstation blocking devices of the MS type). This makes it possible to automate traffic on entire lines.

Equipment of automatic line blocking is used on approximately 1200 km of lines (about 5 percent of all railroad lines). There are six types of these devices. Particularly, for one-direction traffic, which is less efficient than two-direction traffic (...), high operation intensity requires frequent maintenance of the traction network and road surfaces. For this reason it is often necessary to close one of the tracks on two-track lines, and the traffic is then operated in both directions on one track.

In addition, these blocking devices have three positions, with three indications possible on signal lights, namely: "clear way" (green light), "warning" (orange light) and "stop" (red light). When approaching a signal with the "stop" light on, the engineer always first passes a warning signal. In order to increase the traffic capacity of lines with varied types of train traffic, where suburban commuter trains with short braking distance, as well as long-range and freight trains with long braking distance, are used, a four-position blocking will be installed. With a four-position signalization, the engineer approaching a "stop" light will always first see "warning I" (blinking green light), at which he is required to reduce the train speed so as to be able, after passing the indication "warning II" (orange light) at the next light, to stop the train before the "stop" signal.

For automatic train braking, PKP uses throughout its system point-action units acting from the track to the rail vehicle (one-point system SHP).

These devices, installed at certain intervals along the way, monitor the engineer's awareness. Currently in operation are approximately 13,000 track resonators installed on about 15,000 km of lines and approximately 3300 locomotives. The functional capacity of this system is limited, because it cannot control the train braking in a case when the engineer responds automatically to the routine (deactivating the devices by pressing the so-called sensitivity button). So-called active sensors are also installed on locomotives which test the engineer's awareness at regular periods of time. Research is under way to develop a system that could be used for automatic control of trains moving at different speeds. The concept has been tested on a real-size model. Its prototype is being installed on a 20-km line segment equipped with self-activating line blocking system of type Ea. The SHP equipment and active sensors are all based on microchips.

On main lines (about 3000 km), a system of continuous data transmission "track-train" is planned to be installed. This fully electronic system, combined with line blocking and Ea, will supply data to the locomotive which will be analyzed by an onboard computer and used for defining the optimal train speed or activate and monitor the speed at the approach of a stop.

Two systems of remote control of trains are operational in the PKP network. One is used on the Gdansk Main-Gdansk Wistula Port line; it has been developed and installed by the firm Ericsson in the early 1960's; the other operates on the Otwock-Pilawa line and was developed by SOBiRTK and put into operation in 1982. It is based on noncontact remote control devices (BUSZ-H) and a MERA-303 microcomputer. The former system is already obsolete technologically, while the latter represents the state of the art of the late 1960's. There are plans to modernize it with the use of technology of a larger integration scale or microprocessors.

Equipment of traffic control is also used on our railroads; the purpose of this equipment is to improve efficiency of traffic control operators. Three systems are used here: ESKD-72 at the Warsaw hub, ESKD on railroad lines at Trojmiescie and SKD on the Wroclaw-Rawicz line. Technologically, these are information devices which help maintain in good operating order the basic facilities. There are plans to develop and modernize the remote control system on the Otwock-Pilawa line. The operating experience indicates that BUSZ system is efficient. There has been trouble, however, with the MERA-303 microcomputer. It is necessary to standardize the microprocessor equipment used for remote control of vehicles and traffic control.

The protection of guarded track crossings is either automatic (the movement of train causes closing of the crossing) or manual. Until 1980, two systems of automatic crossing signalization were used (COB-588 and COB-63A). The design and components of these units are obsolete, and the systems are no longer being installed. In 1980, the Enterprises of Signalization Equipment at Katowice developed a modernized version of the COB-63A equipment, known as SPA-1 device, which is now being installed on PKP lines. This is a modern electronic and universal system allowing, in particular, to use the capacity for estimating the train speed in controlling a crossing. It can be used in

all operation conditions of PKP traffic. By now, some 150 crossings have been equipped with automatic SPA-1 signalization facilities. There are, however, about 5500 more crossings which are still operated manually. Depending on the traffic intensity and road traffic in the area, these crossings are equipped, in addition, with semiautomatic crossing signalization units SPM-1 which indicate the closing of the crossing by a blinking red light to vehicles on the road (about 1300 units) or signalization devices indicating the approach of the train, SPD-1 (about 200 units). Systems of automatic crossing signalization will be developed. There will be units recognizing the direction of the moving train and measuring the speed of its approach. The automatic crossing signalization SPA-1 will be installed at about 2000 unattended crossings.

In this area our institute is the only research and development unit concerned with the technological problems and introduction of modern technology and methods on Polish railroads. We are developing equipment and testing it, starting from models and continuing on to operation trials. We are also supervising the process of introduction and operation of systems of railroad traffic control.

9922
CSO: 2602/44

ACTIVITIES OF BULGARIAN ACADEMY OF SCIENCES

Information Sciences, Computers

Sofia SPISANIE NA BULGARSKATA AKADEMIYA NA NAUKITE in Bulgarian No 1, 1986 pp 12-16

[Article by Academician Blagovest Sendov: "Information Science and Computer Equipment"]

[Text] It is no accident that information science and computer equipment entered our nation via the Bulgarian Academy of Sciences [BAN] and the Sofia Kliment Okhridski University. On this question there is much to be said and various recollections are evoked in line with the forthcoming celebration of the quarter-century history of the first research center in Bulgaria which arose as a common unit of these two most senior and prestigious cultural centers of our motherland.

At present, Bulgaria has a solid electronics industry and computer equipment is widely employed in managing the economy and production, in scientific research and education. But the pace at which modern computers and information sciences generally are developing is unprecedented. Traditionally this has come about on the basis of the classic sciences of mathematics, physics and chemistry. These sciences also in the future will be the basis of information sciences and computers, but major contributions are also expected in this regard from liguistics and psychology. Here we are not posing the question of what sciences and branches of sciences will be employed by the capabilities of information sciences and computers as this, without exception, involves all sciences in one form and degree or another. What must be emphasized is that for the further development of information sciences and computers, along with mathematics, physics and chemistry, a major role will be played by psychology and linguistics. Certainly here a stipulation must be made. We are mentioning only the basic sciences but we have in mind all their branches such as, for example, mathematical logic, electronics, optics, crystallography, cognitive psychology, mathematical linguistics and so forth as well as the appropriate areas in technology and engineering.

All of this goes to show that in the future the BAN and the Sofia Kliment Okhridski University will play the crucial role in the further development of

information sciences and computers in Bulgaria. Moreover, they are responsible for this development.

1. Multilateral Collaboration

Upon the initiative of the Chairman of the USSR Academy of Sciences, Academician A. P. Aleksandrov, at the end of 1983, the Coordinating Council for Information Sciences and Computers was established for the academies of sciences of the socialist countries. The founding session of this council was organized by the BAN in Sofia and Academician Ye. P. Velikhov, the Deputy Chairman of the USSR Academy of Sciences, was elected its chairman.

The main task of the Coordinating Council for Information Sciences and Computers under the academies of sciences of the socialist countries is to organize and direct collaboration among the fraternal academies related to the development of new generations of computers and the further progress of information sciences.

Collaboration in this area will be carried out according to individual plans and will be implemented through the base laboratories with international participation.

For carrying out our obligations in this area, under the BAN the following base laboratories have been established for:

a) Highly productive architectures and algorithms;

b) Networks of computer systems;

c) New principles for external storage devices;

d) Training information science.

The last laboratory is based upon the Special-Problem Group for Education Under the BAN and the Ministry of Public Education.

2. The Evolution of Computer Structures

2.1. Technologies for Automatic Computing.

It is well known that the idea of automatic computation which is the very heart of information sciences and computers is very old. It goes back to the famous English mathematician C. Babbage who at the start of the last century designed his "calculating engine" and established the foundations of automatic calculation. But Babbage did not possess the suitable equipment for carrying out the calculations. He attempted to construct his engine from metal and naturally did not reach satisfactory results in spite of his amazing tenacity. This history is very instructive as an example of an idea which in time greatly outstripped the actual capabilities for its application. At the end of the 1930's, the American mathematician and theoretical physicist of Bulgarian origin G. Atanasov ventured to use a flow of electrons in vacuum tubes as the calculating technology. The metal gear of Babbage with a

precisely determined finite number of possible positions for determining the value of the figures which were being calculated was replaced by Atanasov with two possible states of an vacuum tube corresponding to the two possible values of one binary digit.

The electronic technology in automated calculation has up to now gone through several stages of decisive improvement. The physical phenomenon which rests at its basis is the control of a more powerful flux of electrons by another weaker flux. The great progress in converting from vacuum tubes to transitors, integrated circuits, large integrated circuits and super-large integrated circuits is due to the improvement in the production methods and the development of the possibility of realizing this main phenomenon of controlling one flux of electrons by another flux of electrons in an ever-smaller physical volume and at an ever-lower price.

The natural question here is the following: are other technologies possible for realizing automatic calculation and which have certain advantages over electronic technology? The natural candidate for replacing the flux of electrons in automatic calculation is a flux of photons or a light beam. Even the light analog of the electronic transistor is already known as the transphasor. The future achievements of physics and chemistry will provide the answer to the above question. Not to be excluded is the possibility that certain ideas will also come via biology.

Just as for G. Atanasov it was difficult to reach the idea of replacing a metal wheel by an electronic flux so at present it is hard to imagine another carrier of rapid automatic calculating which differs from the electron flux. Even the capabilities of electronic technology in automatic calculating are far from exhausted. But, on the other hand, there are grounds to feel that this is the best and irreplaceable one.

2.2. Architectures of Automatic Calculation.

Automatic calculating machines have a specific structure, or, as we have come to say, an architecture which carries out their functioning. Characteristic of the first automatic calculating machines was that the processing of information in them, the calculating, was done in a single sequence. The essential arithmetical and logical operations were performed one after another. Although the time for performing a single operation was reduced by improving the electronic elements, the desire to obtain ever-higher speeds and greater productivity of the computer systems has led to the introduction of parallelism in the architectures of modern calculating machines.

Widely employed is the classification of M. Flynn of various types of parallelism in computer systems. With this classification, the physical differences are not taken into account but rather the relationship between the instructions performed at the given moment and the units of information to which these instructions are applied. M. Flynn has proposed the following three types of calculating machines:

a) SISD (Single Instruction Stream/Single Data Stream). Machines of this type are without parallelism. At each moment the machine performs one

instruction on one binary digit or a given unit of information. This was the machine conceived of by Babbage and a predominant majority of modern electronic calculating machines;

b) SIMD (Single Instruction Stream; Multiple Data Stream). In these machines there is parallel data processing. Various flows of data move in parallel and they pass through the corresponding arithmetic devices. But in each individual cycle of machine operation, all the arithmetic devices perform the same instruction. Typical SIMD machines are the matrix processors which are very convenient for calculating vectors. In the addition, subtraction and scalar multiplication of vectors, the same arithmetical operation is performed with different components of the vector;

c) MIMD (Multiple Instruction Stream; Multiple Data Stream). These are parallel machines in the full sense of the word because in each cycle individual arithmetical devices perform different operations on different data. In essence, the MIMD machines are a complex of SISD machines which have a direct connection between themselves.

Naturally, the most progressive structure is the MIMD, but it requires concretization. Of great importance is the structure of the links between the individual components in one such machine.

Very new and difficult-to-solve questions arise in realizing and using parallel-architecture machines. The parallelism is required by the need to increase machine productivity. But it is very difficult to achieve a 100-fold increase in the productivity of one non-parallel machine by one machine which contains 100 parallelly operating processors. The achieving of high productivity with parallel machines depends upon to what degree their structure conforms to the specific features of the problem being solved. For this reason, one can expect a return from universal machines to a certain specialization conforming to the nature of the mass-solved problems.

Of great importance in relation to the productivity of the different structures of parallel machines is the studying of abstract machines with differing architecture and the theoretical examination of their characteristics. A new area arises in numerical methods in which estimates are made concerning the quality of the numerical algorithms from the viewpoint of their realization by different computer architectures. The possibility of deparalleling the given numerical algorithm is a new quality which will be evaluated in the parallel calculating machines. It is naturally expected that in the future fundamentally new architectures of computer systems will be developed.

2.3. Contact with Automatic Transformers.

The mass use of automatic calculating machines (or automatic data transformers) requires the evermore convenient and unobstructed communication of people with them. For this purpose, so-called algorithmic languages are developed. These languages have a very strict syntax and limited opportunities for expression. Their study to the point of their free employment in operating the machines requires special training. For this

reason, quite naturally the desire has arisen to teach the machines to understand natural human language, written or spoken. A program announced at the beginning of the 1980's in Japan for developing the fifth generation computer systems includes the realization of this desire. It has been asserted that before the middle of the 1990's, machines will be developed which can understand all natural human language. These ambitions are linked to the possibilities of simulating and modeling human intelligence (or, as is said, the developing of artificial intellect).

The solving of the problem of the automatic processing of information provided by natural human language requires a very profound understanding of natural languages from the generative and structural viewpoint. For this reason, linguistic and psycholinguistic theories and knowledge assume particular importance. Previous experiments on automatic translation from one language to another natural language have shown a number of bottlenecks which still have not been overcome. It is important to point out that in addition to the common problems of all natural languages, for each individual natural language there are its own specific problems which must be studied and solved individually if one desires to use it for exchanging data with an automatic calculating machine. These particular features of each separate language must be understood also with the more humble and limited applications of a living language for automatic data processing. All of this imposes particular responsibility for the BAN and the Sofia Kliment Okhridski University in organizing and conducting the corresponding research of the Bulgarian language for the needs of automatic data processing. Certainly this is not a question which is scarcely being raised only now. Work has been in progress on it for a long time but its great importance for the future development of information sciences and computers obliges us to pay it much greater attention with human and material resources.

3. Information Metaphors

The second half of our century is characterized not only by the broad invasion of evermore advanced computer systems and the mass application of automatic data processing into practice. At present, we are inclined to explain the world by information metaphors. Most characteristic in this regard is the example of modern biology. Genetic theory which has provided such rich fruit describes vital processes as processes of the encoding, decoding and transmitting of information.

Modern psychology finds good support in the model of the functioning of the human brain constructed by analogy with a computer. Or more precisely, the difficulties which are encountered in attempting to model the activities of the human brain by a computer provide food for new hypotheses in terms of the brain's operating mechanisms.

Very frequently voices are heard which state categorically that information machines will never attain the capabilities of a person as a thinking being. In a rhetorical argument scarcely anyone would be able to prove the opposite. Much more important and irrefutable is that man armed with a computer will be unattainable in terms of capability by a man without a computer. Here we must draw attention to one other aspect of the presence of the computer. Our

attempts to construct evermore complex and more advanced computers can help us penetrate more profoundly into the mechanisms controlling the work of the human brain. Today it is clear that the processing of information in the human brain does not occur as it does in computers. This is apparent from a simple comparison of the capabilities of a man and a computer. A computer calculates very quickly and accurately with a large amount of digital data. In this regard, it surpasses a man by thousands and millions of times. On the other hand, a man very quickly and easily processes image information. For example, a computer cannot rival a man in any way in identifying human faces. A computer does many things involving the processing of information much more slowly than man or cannot do this at all. This has provided the grounds for a popular definition of artificial intelligence. A problem is considered a concern of artificial intelligence if this problem is easily solved by man, while a computer finds it very difficult to solve it or cannot solve it at all.

This difference in the capabilities of man and the computer is a good prospect for their collaboration and reciprocal complementing. But the desire and aspiration to overcome the difficulties in developing the computers and the programs for these computers which simulate the typical capabilities of the human brain will help in better understanding the human brain itself. For this reason of particular importance is the work being done by psychologists from the standpoints of information sciences.

Chemical Engineering

Sofia SPISANIE NA BULGARSKATA AKADEMIYA NA NAUKITE in Bulgarian No 1, 1986 pp 23-27

[Article by Corresponding Member Dimitur Elenkov: "The Development of Chemical Engineering in the BAN"]

[Text] Chemical engineering arose and developed as an independent scientific area at the beginning of the 20th Century as a result of the weaknesses in the technological approach to studying the chemical production facilities of the chemical industry and similar sectors. While with the technological approach the industrial facilities were ranked and studied according to the types of production and lines, chemical engineering, in using recent achievements in mechanics, physics, chemistry, biochemistry and mathematics, classified the facilities according to their basic physicochemical essence, providing general (standard) methods for their study, choice of application, intensification, designing and optimum control and proposing new promising processes and facilities for use by industry. Its advances were closely tied to the development of modeling theory which is the basic method in chemical engineering for the rapid, secure and inexpensive transfer of laboratory scientific experience into industry. And the latter, as is known, is one of the most complicated, most difficult and most important problems in introducing scientific achievements into production.

The bases of chemical engineering in the BAN were established in 1961 with the creation of the Section for Mass Exchange Processes Under the Institute for General and Inorganic Chemistry at the former Department for Chemical

Sciences. By so doing, the BAN outstripped many foreign academies. A new step was taken in 1972 with the turning of this section into the Central Laboratory for Theoretical Principles of Chemical Engineering (TsLATOKhT) under the Unified Center for Chemistry. It has four separate laboratories: the Laboratory for Mass Exchange Processes which has taken over, continued and broadened the problems of the Section for Mass Exchange Processes; the Laboratory for Chemical and Biochemical Agents with the scientific problem of investigating chemical, chemical engineering and biotechnical agents; the Laboratory for Modeling and Optimization with the main problem of chemical production systems; the Laboratory for Large-Scale Laboratory Experiments for testing certain models and installations under conditions which are close to industrial ones, and a small computer center.

The fundamental and applied scientific interests of the TsLATOKhT collective have been united in a single scientific problem: "Modeling, Intensification and Optimization of Chemical Production and Bioengineering Installations" and which is recognized on a national level and for which the laboratory is the coordinator of fundamental research in the nation.

In a fundamental aspect, the scientific interests of the laboratory are focused on a study of the mass exchange and energy processes in the most frequently encountered objects in industry such as flowing films, drops and bubbles, on the one hand, and the hydrodynamics and mass exchange in intensely working devices, chiefly the Venturi tube, columns with packing, extractors with external energy and others, on the other. What are the most important scientific achievements in this area? It has been established that in the laminar flow of films, there are areas along their length in which the velocity fields differ substantially depending upon the effect of the superficial forces. A study of the breaking up of a disperse phase (drops) in intensely operating industrial mass exchange equipment has shown that the atomization is subordinate to Kolmogorov's law and that the deviation from it observed in certain instances is due to polluting by surface-active sediments. Our research on the effect of phase velocities and the presence of impurities with surface-active sediments on mass exchange in various designs of Venturi tubes has shown that this type of equipment can be successfully employed as intensive absorbers and extractors (particularly if the phases foam). The hydrodynamic picture and mass exchange were studied and clarified in great detail under pure conditions and in impurities with surface-active sediments in the most mass employed absorption and extraction equipment in industry, the columns with packing. Incidentally, an integrated investigation of the influence of surface-active substances on the hydrodynamics and mass exchange in fluid-fluid systems, in terms of its comprehensiveness of investigation, originality of methods and particularly in terms of the scientific achievements, have provided grounds for certain foreign scientists to consider this Bulgarian.

A number of extraction processes has been developed, namely those for extracting various valuable metals from industrial waters on the basis of the studied exchange mechanism between metal cations and various chelating extractants and for removing volatile oils and other valuable organic products from waste water.

In addition to this, a theory has been elaborated for the transfer of matter through selective fluid membranes and a new separation process (pertraction) has been proposed using creeping films. The process has universal application and as a standard production method can be employed in the chemical and food industry, hydrometallurgy, medicine and so forth. The new method has been patented in a number of technically advanced countries and is included in the Bulgarian export list.

On the basis of a system of differential equations for a model of ideal substitution, a method has been developed for calculating combined heat and mass exchange in columns with packing with condensation and evaporation and this makes it possible to predict the formation of mist as a consequence of the heat and mass exchange.

In the area of chemical agents, new light has been shed on the phenomenon of segregation and kinetics of heterogeneous catalysis for industrial purposes. Jointly with the catalysis institute of the Siberian Division of the USSR Academy of Sciences, on a macro level we have investigated the course of catalytic oxidation of sulfur dioxide to sulfur trioxide under non-standard conditions and the combustion of organic harmful components in the waste gases from the chemical, metallurgical and food industries and this has broadened the use of this method under industrial conditions.

The grounds for us to begin bioengineering research in recent years were not only the timeliness of the problem but the fact that with biotechnical objects energy and mass exchange are the basis and here the laboratory has acquired scientific experience as well as the fact that the chemical engineering approach is the most promising. Our fundamental research on the kinetics of the conversion of sorbite into sorbose and of the sorbose into L-ascorbic acid (vitamin C) has provided qualitatively new information on the course of this process and this is of great technological interest.

We have designed an original, patented, bioreactor of the airlift type with a reverse fluidized bed for an active biomass spontaneously fixed on a solid carrier with great possibilities (particularly for the treating of industrial waste water).

In order to meet the needs of intensive development in our chemical industry by optimum reconstruction and modernization of the existing chemical production systems (CPS) using the methods of mathematical modeling, the collective of the Laboratory for Modeling and Optimization has developed a new area for world scientific practices of CPS rennovation, that is, bringing the existing CPS to a new state which is economically more efficient in comparison with the old. For this purpose they have developed methods, algorithms and the program systems for the optimum synthesis of CPS with reduced energy consumption. Several patented production designs have been worked out. In addition, programs have been developed which are the chief elements in the programs for encouraging the CPS. One such program, for example, is a mathematical model of a pyrogas compressor for oil refining. The model encompasses the entire program unit and contains 114 devices with 187 flows between them.

As for the importance of the scientific achievements of the TsLATOKhT, let me give two facts:

1. The laboratory has over 250 scientific papers and publications in the most prestigious Bulgarian and foreign (USSR, CSSR, GDR, Hungary, Poland, France, England, Belgium, Sweden, the United States and Canada) scientific journals and these are repeatedly quoted in textbooks, collections, monographs and foreign scientific papers. Of the papers published in Bulgaria, nine have been completely translated and printed in the American journal INTERNATIONAL CHEMICAL ENGINEERING where they select only the best works in chemical engineering printed not in English but in a foreign language.

2. The laboratory is a permanent partner and collaborates in Bulgaria with the Chair for Chemical Engineering Under the Higher Chemical Engineering Institute in Sofia, the Scientific-Research Chemical Pharmaceutical Institute, Farmakhim [Pharmaceutical-Chemical Trust], the Sector "Ecological Microbiology" of the Biological Faculty Under the Sofia Kliment Okhridski University and Khimproyekt [Chemical Design Institute], and abroad with the Institute for Heat and Mass Exchange imeni Likov Under the Belorussian Academy of Sciences in Minsk, the Catalysis Institute of the Siberian Division of the USSR Academy of Sciences, the Institute for the Theoretical Bases of Chemical Technology Under the CSSR Academy of Sciences, the Institute for Technical Chemistry Under the Hungarian Academy of Sciences at Veszprem, the Chemical Engineering Institute in Toulouse and the Technical University in Bochum (FRG) as well as with the Higher Polytechnical Institute in Montreal, Canada.

The applied scientific and introductory activities of the TsLATOKhT are closely tied to its fundamental research and are most often its result. Thus, as a result of our fundamental research, a number of dependences were provided for engineering calculations and new designs for working elements (fillers in the form of elastic sheets, honeycomb, a beveled "Raschig ring," a pulsator and so forth) as well as patented equipment most of which has been put into production.

In addition to this, the applied scientific and introductory activities of the TsLATOKhT are no less successful and effective than the fundamental research due to the following factors of a fundamental nature:

1. To a large degree the laboratories of the TsLATOKhT are of an arbitrary nature. Its scientific collective has been grouped into four laboratories according to scientific interests and problems but the physical plant is a common one. Moreover, in order to carry out a major applied scientific task which requires numerous different forces in terms of scientific preparation, as was the case with the development of the new, economically effective and waste-free production method for integrated hydrometallurgical processing of our concentrates (or the reconstruction and putting into operation of a shop for the recovery and reclaiming of carbon disulfide from the gases of the converters at the Sviloza Chemical Economic Combine in Svishtov), an interdisciplinary scientific collective was organized regardless of laboratory affiliation for its members. In this regard, the TsLATOKhT already has certain experience in the establishing and functioning of specific program collectives.

2. The collective of the TsLATOKhT is capable of accepting the obligation of a complete solution to a given problem, in conducting the laboratory research, providing a preliminary concept, a design specification, and exercising developer supervision in the designing and manufacturing of the equipment; if the design organization is unable to design the given assembly, the institute designs it; it participates in the installation and the starting up of the project.

The applied scientific interests of the TsLATOKhT collective date back to the founding of chemical engineering at the BAN. In 1962, the leadership of the G. Dimitrov State Mining and Metallurgical Enterprise in Eliseyna asked it to reconstruct a derelict chemical shop, in providing a new more modern and more economic production method which would more completely recover the valuable components from the plant's converter gases. This meant completely new production methods and a shop. In utilizing their experience and achievements from fundamental research on the Venturi tube, the collective of the then Section for Mass Exchange Processes worked out a fundamentally new, patented production method which recovered and utilized the lead and copper aerosols and the sulfur dioxide. The collective participated in the design and starting up of the shop in 1965. In 1968, a second shop was put into operation at the Lead-Zinc Plant in Kurdzhali. These two industrial units are functioning without problem as present.

In 1978, the Ministry of Chemical Industry asked the TsLATOKhT to reconstruct and put into operation a shop for the recovery and regeneration of carbon disulfide from the waste (ventilating) gases at the converters of the Sviloza Chemical Economic Combine in Svishtov and which had been built in 1971 by the West German BAMAG firm but was not operating.

On the basis of three patents and an original filler (honeycomb), the TsLATOKhT collective designed a new absorption unit for absorbing the hydrogen sulfide carried by the gases, and it studied, reconstructed and put into operation a shop for the recovery and regeneration of the carbon disulfide. An economic effect of 1,269,000 leva was realized just from the savings in capital investments on the collective's absorption unit.

These two developments, in addition to the recognized great economic effect, have also had a major ecological effect from the preservation of the environment.

Using a horizontal sheet packing, two of our machine building plants are producing highly efficient deaerators for the needs of the Ministry of Power and primarily for export. The new deaerators are on the highest technical level, they have a much smaller working volume than the old ones and the "K" [Quality] mark, they have found good acceptance in the nation and abroad and have brought the national economy a significant savings in metal with a foreign exchange return rate of 400 percent.

On the basis of the developed designs for packing and spraying devices, a new highly effective contact economizer has been developed and tested for the recovery of fuel from flue gases and this has significantly surpassed the

known equipment of this type and is in the process of being introduced at the Sofia TETs [thermal power plant].

According to designs of the TsLATOKhT, cracking towers have been introduced for purifying aniline and removing methanol from formaldehyde and a drying tower at the Chemical Economic Combine in Dimitrovgrad. Installations for scrubbing the gases and the recovery of waste fuel are in the process of being introduced at the Razlog Pulp and Paper Combine and so forth.

The two AROMEKS installations put into operation in 1984 have doubled the production of varnish linseed oil in the Farmakhim system. A KOMEKS installation has also been introduced.

The collective from the Sector "Modeling of Chemical Engineering Systems" together with the Department for the Automating of Engineering Activities Under the Chemical Complex has developed SIMULA, THERMSU, EQUILIBRIA and TERMEFF automated program systems and these operate in a dialogue mode and have been put into production practice. This has led to a rise in the quality of engineering work and represents a base for building an integrated system for automated designing.

The collective from the same sector of the TsLATOKhT has worked out and introduced at the D. Toshkov Chemical Economic Combine a PLAST dialogue program system for operational control of the installation producing plasticizers. The system can be employed on different levels (from a production engineer to the director in chief), without the need to know the computer programming. Its introduction represents a substantial intellectualization of engineer work and leads to a sharp rise in the quality of operational management.

There is a proposal to reconstruct the distillation unit at the isomerization installation at the Neftokhim [Petrochemical] Chemical Economic Combine. The technical and economic studies made at Neftokhimproekt [Petrochemical Design Institute] on this proposal have shown an expected economic effect of 5,126,000 leva with a repayment time of 2 years and 1 month for the capital investments. Other proposals relate to the reconstruction of an oil deparaffination unit and an electric desalination installation at the atmospheric-vacuum distillation shop at the Pleven Petrochemical Combine and also have a significant expected economic effect.

As a result of the applied scientific developments during the Seventh Five-Year Plan the TsLATOKhT has a proven economic effect that is double the laboratory's budget for this time, and during the Eighth Five-Year Plan this will be even greater.

For the designated developments the members of the TsLATOKhT have repeatedly been awarded honorary titles and insignias.

Sofia SPISANIE NA BULGARSKATA AKADEMIYA NA NAUKITE in Bulgarian No 1, 1986 pp 63-65

[Article by Mariya Grozeva: "The 14th Conference of Representatives From the Academies of Sciences of the Socialist Countries"]

[Text] From 24 to 27 September 1985, the 14th Conference of Representatives From the Academies of Sciences of the Socialist Countries was held in Warsaw, Poland. Participating in the work of the conference were delegations from the BAN, the National Center of Scientific Research and the Committee for Social Sciences of Vietnam, the GDR Academy of Sciences, the Cuban Academy of Sciences, the North Korean Academy of Sciences, the Mongolian Academy of Sciences, the Polish Academy of Sciences, the Romanian Academy, the USSR Academy of Sciences, the Hungarian Academy of Sciences and the CSSR Academy of Sciences, with the scientific secretary of the Afghan Academy of Sciences and a deputy secretary from CEMA present as observers.

The 14th Conference of Representatives From the Academies of Sciences of the Socialist Countries was opened by the welcome of the Scientific Secretary of the Polish Academy of Sciences [PAN], Academician Z. Kaczmarek. As a representative of the host academy, he was elected the permanent chairman of all the sessions.

Those present heard and approved the report of the PAN which is the organizer of multilateral collaboration concerning the results of collaboration over the period of 1981-1985 and on the carrying out of the decisions of the previous conference. It was pointed out that during the period between the 12th and 14th Congress, multilateral cooperation was widened, with the establishing of the Coordinating Council for Computers and Information Sciences and two new special-problem commissions "Electrochemistry" (coordinator, the Central Laboratory for Electrochemical Current Sources Under the BAN) and "The Physiology of Visceral Systems" (coordinator, USSR Academy of Sciences).

The participants at the conference stated that the results achieved within the framework of the special-problem commissions and the international centers, in carrying out their scientific programs, have been on a high level, and over 1,000 collections and monographs had been published reflecting the results of the scientific research, a large number of conferences and symposiums had been held on an international level, and patents and certificates of invention had been obtained with great practical application. The academies of sciences and the special-problem commissions are making systematic efforts to improve the organization of multilateral collaboration and to increase its effectiveness. Participation by scientists from Vietnam, North Korea, Cuba and Mongolia in specific joint projects is growing stronger and becoming more active. However, along with the successes, attention was drawn to shortcomings in the work of certain special-problem commissions.

It was decided that the chairmen of the special-problem commissions in the area of natural sciences would prepare information on the completed joint research during the 1981-1985 period when the results can be introduced into

practice, and beginning in 1986, this information will be made available to the CEMA Secretariat and to all the academies of sciences participating in multilateral collaboration.

Heard with great interest was the report of Prof O. A. Rzheshevskiy (USSR Academy of Sciences) on the subject "Forty Years From the Victory Over Naziism." This brought out the historical importance of the victory of the peoples over the Nazi aggressors, the decisive role of the USSR in this victory, and its influence on the change in the sociopolitical situation in the world and the establishing of socialism as the leading force of modern development.

After this, reports were reviewed on the activities of certain multilateral collaboration bodies including the Special-Problem Commission on "Molecular Biology" and the St. Banach International Mathematical Center (headquartered in Warsaw, Poland). The participants in the conference had very strong praise for their activities and made certain recommendations on their future work.

The delegation members were acquainted with information on the course of work on the Interdisciplinary Program for Scientific-Technical Progress in the CEMA Member Nations Up to the Year 2000. They affirmed the interest and readiness of their academies to participate in its implementation. Proceeding from the task which the parties and governments of the fraternal countries have posed for converting the national economy to intensive development on the basis of accelerated scientific and technical progress, the delegations attending the conference emphasized the need to continue the coordinating of scientific policy and the elaboration of a program for multilateral collaboration over the longer run.

The report was approved on the work carried out by the academies of sciences related to implementing the Long-Range Program for Multilateral Collaboration in the Area of Natural Sciences for the Period of 1981-1985.

Note was taken on the thorough work carried out by the special-problem commissions to prepare the special-problem plans for 1986-1990 and which clearly outlined the aims and expected results and which anticipate the changeover to such effective forms of collaboration as plans and specific programs.

At the conference it was decided to continue the work related to long-range planning of multilateral collaboration in the area of the natural sciences and to begin working out a new long-range program for the next 15-20 years, with the draft of this program being worked out by a new organizer academy of multilateral collaboration with the help of the remaining academies.

The conference participants adopted the Program for Multilateral Collaboration in the Area of Natural Sciences for the Period of 1986-1990.

It was resolved to establish a permanent coordinating conference of the academies of sciences of the socialist countries on spectroscopy, with the USSR Academy of Sciences being approved as its coordinator.

In line with the recommendation of the Conference of Leaders From the Departments of Physical Sciences of the Academies of Sciences of the Socialist Countries, it was resolved to supplement the Program for Multilateral Collaboration in the Area of Natural Sciences for the Period of 1986-1990 with the problem "The Physics of Surfaces," with the USSR Academy of Sciences also being established as its coordinator.

Those present approved the request sent to the organizer academy (the GDR Academy of Sciences) to organize in the 1986-1987 period a conference for the chairmen of the special-problem commissions for natural sciences to discuss the scientific and organizational questions.

The BAN delegation presented information on the work and decisions of the Sixth Conference of Deputy Chairmen for Social Sciences of the Academies of Sciences of the Socialist Countries held in 1984 in Sofia. Thanks were expressed to the BAN for the work done in preparing and holding this high and responsible forum. The participants were informed that the BAN had assumed the obligation of preparing a draft of the Long-Range Program for Multilateral Collaboration in the Area of Natural Sciences. This draft was discussed at the First Conference of the Chairmen of Special-Problem Commissions for Natural Sciences which was held in Sofia from 18 to 22 November 1985 and after this was submitted for approval to the Seventh Conference of Deputy Chairmen for Social Sciences of the Academies of Sciences of the Socialist Countries in April 1986 in Cuba.

The conference heard information from the scientific secretary of the Afghan Academy of Sciences on the activities and tasks of the academy.

The question was discussed of coordinating the activities of the Coordinating Council for Computers and Information Sciences and the Coordinating Committee for Scientific Instrument Building and the Automating of Scientific Research. The conference participants recommended the reciprocal membership of the representatives in the work of these bodies in the aim of carrying out joint research and measures.

The PAN delegation provided information on a concept for establishing an international center for biocybernetics for the academies of sciences of the socialist countries with headquarters in Poland as well as a paper concerning the work of the journals SCIENCE OF SCIENCE and NAUCHNAYA APPARATURA [Scientific Equipment].

Those present took into consideration and welcomed the statement of the North Korean Academy of Sciences on adhering to the treaty concerning the establishing of the St. Banach International Mathematics Center and the agreement to establish an International Center on the Problem "Heat and Mass Exchange."

Lastly, the general secretary of the Cuban Academy of Sciences proposed that his academy would host the 15th Conference of the Representatives From the Academies of Sciences of the Socialist Countries in Cuba in 1987.

The general secretary of the GDR Academy of Sciences expressed the readiness of his academy to assume the function of the organizer of multilateral collaboration over the 1986-1987 period.

The conference approved the minutes reflecting its decisions and these were signed by the delegation leaders.

The 14th Conference of the Representatives From the Academies of Sciences of the Socialist Countries was held in a friendly atmosphere and on all major questions full unanimity and agreement on views and approaches were reached.

Materials Conference

Sofia SPISANIE NA BULGARSKATA AKADEMIYA NA NAUKITE in Bulgarian No 1, 1986 pp 70-73

[Article by Senior Science Associate Konstantin Yamboliev: "The Fourth National Conference With International Participation on the Mechanics and Technology of Composite Materials"]

[Text] For the fourth time running, the Central Laboratory for Physicochemical Mechanics Under the BAN from 2 to 4 October 1985, at the Druzhba Resort near Varna, held a national conference with international participation on the subject "Mechanics and Technology of Composite Materials." The conference is held every 3 years. This time, participating as co-organizers were the Union of Scientific Workers in Bulgaria, the Section "Technical Sciences" and the unions for construction and for chemistry and the chemical industry under the Central Council of Scientific-Technical Unions in Bulgaria.

The conference was opened by the chairman of the Organizing Committee, Corresponding Member Yordan Simeonov, director of the Scientific Trust for Basic Problems of Technical Sciences and the Central Laboratory for Physicochemical Mechanics Under the BAN. The Scientific Secretary of the BAN, Senior Science Associate Ya. Ivanov, read the welcome to the delegates and guests of the conference on behalf of the Honorary Chairman of the Organizing Committee, Academician A. Balevski and Chairman of the BAN.

The mass application of composite materials in all spheres of life has brought about the great development of scientific research in the area of composite materials in recent years in all developed countries. A study of the factors which determine the regulation and control of structure-forming processes is the crucial condition for obtaining new materials with preset physicomechanical properties.

The rational and efficient use of composite materials in our country has led to the saving of materials, raw products, energy and fuel and this has been the main requirement of the 12th BCP Congress and the February Plenum of the BCP Central Committee (1985). The Central Laboratory for Physicochemical Mechanics Under the BAN has been entrusted with the functions of coordinating the fundamental and applied research in the area of non-metallic composite materials in our country. For this reason every 3 years it holds a national

conference with international participation, in the aim of reviewing the achievements in the area of the mechanics and technology of non-metallic structural composite materials over the last 3 years in Bulgaria and at the same time elucidate the current state of the problem in other countries. Focusing on this aspect was the greetings of Academician A. Balevski read at the opening of the conference and published in the given collection of papers.

The Fourth National Conference on the Mechanics and Technology of Composite Materials was held in two sections.

1. Mechanics and technology of structural polymer composite materials;

2. Mechanics and technology of structural silicate composite materials.

These two sections included the following scientific areas:

A. Rheology of fluid compositions;

B. Structure, properties and production methods.

Participating in the work of the conference were 191 scientific workers and specialists including 56 persons from the USSR, Poland, the GDR, CSSR, Hungary, the FRG and Great Britain. Also present were representatives from the internationally renowned International Conference on Building Materials and Silicates IBAUSIL, from Weimar, GDR, Docent, Dr H. Keller and Dr R. Hutschenreuter. The Central Laboratory for Physicochemical Mechanics has concluded an agreement on collaboration with this conference.

Participation in the conference by representatives from so many countries is indicative both of the great interest shown in the question as well as recognition of the scientific achievements and employment of composite materials in our country.

Bulgarian participants represented 7 academy organizations, 5 institutions of higher learning, 15 scientific research, engineering and design institutes, 2 ministries, 11 trusts, combines and plants.

The main report on the achievements of the mechanics and technology of composite materials in Bulgaria over the last 3 years was given by Corresponding Member Yordan Simeonov and has been published in a collection of conference papers. It generalized the results of the scientific research and use of non-metallic structural composite materials. Also given were the accomplishments in studying the rheological behavior of fluid-disperse compositions such as cements, mortars and concrete mixes, the processes of structure formation and the properties of non-metallic structural composite materials based on polymers and silicates. The report also pointed out the research conducted in our nation on the production processes in obtaining composite materials as well as the methods of their improvement.

Individual problems in the broad area of composite materials were the subject of the 7 plenary reports given at the conference by Corresponding Member Yordan Simenonov (Bulgaria), Academician F. D. Ovcharenko, Corresponding

Member of the USSR Academy of Sciences, Prof Yu. S. Urzhumtsev, Prof N. V. Churayev and Prof A. A. Berlin (USSR), Academician J. Nemec (CSSR) and Prof U. Ludwig (FRG).

The great role played by additives in improving the properties of composite materials was taken up in the plenary report of Corresponding Member Jordan Simeonov. The achievements of the Central Laboratory for Physicochemical Mechanics were set out in the area of investigating certain additives the use of which significantly improves cement qualities. It was emphasized that the introduction of these additives leads to the saving of energy with a great economic effect.

The problem of optimum designing with a discrete range of materials of laminated elements and surfaces of composite materials was taken up in the plenary report of Corresponding Member Yu. S. Urzhumtsev. These elements and surfaces exposed to waves of varying physical nature have found great application not only under the conditions of the Soviet North but also in all areas of life.

Research on the long-term processes of change which occur in the composites with a polymer matrix as a consequence of fatigue was described in the plenary report of Academician J. Nemec. Changes in the property of polymer matrices which occur under the conditions of a long-term load are particularly important from the view of employing them. The report also described an original research method.

The structural-rheological properties of disperse systems and the forecasting of changes which occur in them in a change in the composition of the disperse medium can be explained by research on the surface forces and the flowing of fluids in the delicate layers and pores. The plenary report of Prof N. V. Churayev was devoted to these questions.

The plenary report of Prof U. Ludwig analyzed the effect of various types of additives for cements and concretes from the viewpoint of achieving a savings in materials and energy in employing them.

Research on the plastic properties of polymer matrices and their influence on the strength of reinforced polymers was set out in the report of Prof A. A. Berlin.

Interest was shown in the reports of Prof V. A. Voznesenskiy (USSR) and Senior Science Associate Ya. Ivanov (Bulgaria) and collectives, in reflecting present-day theoretical and experimental research on the effect of polydispersion and granulometry of additives on the rheological properties of polymer binding and hardening compositions. On this same scientific area "Rheology of Fluid Polymer Compositions," reports were given dealing with research on the rheological properties of fluid polymer compositions. Such were the reports of Prof N. N. Krulitskiy (USSR) and collective and Senior Science Associate B. Dzhagarova (Bulgaria) and others.

In the scientific area "Rheology of Fluid Silicate Compositions" the reports given reflected the following more important questions: "Structure Formation

in Disperse Composite Materials Considering the Dynamics of Contact Interactions" (B. B. Uriyev, USSR), "Rheological Measurements As a Means of Monitoring Concrete Quality" (P. Banfill, Great Britain), "Rheological Properties of Suspensions With a Disperse Phase of Heavy Mineral Particles" (E. Krusteva, et al., from Bulgaria) and others.

A total of 49 papers were given in the scientific area "Properties and Technology of Structural Polymer Composite Materials" and these reflected the following more important questions: the influence of a cyclical load on the adhesive strength of glass-filled thermoplasts (I. Sgureva, et al., from Bulgaria), long-term strength of brittle material with an interior disk-shaped cracks (K. Popov, et al., from Bulgaria), the trizonal structure and strength of integral foam plastics (F. Shutov, USSR). In the area of research on polymer concretes, the following questions were examined: the influence of structural parameters on the creep of a polymer-concrete matrix (Yu. Khristova from Bulgaria), the dependency of the amount of stress of a polymer concrete matrix and its adhesion to metal threads (K. Yamboliev from Bulgaria), the influence of certain additives on the histeresis properties and corrosion resistance of polymer concrete (N. Gudev, et al., from Bulgaria) and so forth. Various questions from research on polyethylenes were taken up in the reports of M. Natov, et al., L. Peeva, et al., L. Bozveliev, et al. (all from Bulgaria). In certain of the given reports, methods were examined for obtaining and describing new composite materials such as: metallopolymers (Yordan Simeonov, et al., Bulgaria), polypropylene compositions (P. Komitov, et al., Bulgaria), packing composite materials for sealing high-strength bolt joints (M. Aladzhem, et al., Bulgaria), composites with hybrid reinforcing (I. Izbicka, Poland) and others.

Present-day research on improving the properties of silica-base composite materials and obtaining new ones was the subject of the reports given in the scientific area "Structure, Properties and Production Methods" under the Section "Mechanics and Production Methods of Structural Silicate Composite Materials." Research on structure formation and its control as the determining property of a composite material was set out in the reports of: V. F. Yanchikov (USSR), on the structure, hardening and destruction with heat curing of haydite cement; I. Yanve, et al. (Bulgaria) on the structure of cement stone; G. Bozhinov, et al. (Bulgaria) on the phase composition of cement stone hardened in sea water and so forth. Research on the establishing of the physicomechanical and technological properties of concretes was the subject of reports by Yordan Simeonov, et al. (Bulgaria), N. Dzhabarov, et al., B. Darakchiev, D. Nazurski, et al., all from Bulgaria, Z. K. Tsilosani, et al., V. A. Lobkov, et al., A. P. Pak, et al., all from the USSR and J. Jaworsky, et al. (Poland). One part of the reports in this scientific area had as its object the problem of improving the properties of concrete and natural stones by treating them with polymers. These were the reports of Yordan Simeonov, et al., S. Milkov, et al., all from Bulgaria; M. Bodnar, et al., T. Broniewsky, et al. (Poland); S. Slanicka, et al. (CSSR). The development of new types of cements and concretes and the methods of obtaining them are an evermore developing area in the production of silicate materials. This problem was the subject of reports by Yordan Simeonov, et al., V. Vulkov, et al., I. Vulkova, et al., L. Bozadzhiev, et al., N. Karapchanski, et al.,

all from Bulgaria; Yu. D. Chistov (USSR), W. Muszinsky, et al., L. Rudzinsky, et al. (Poland).

A larger portion of the reports represented at the conference were written in one of the working languages -- Bulgarian, Russian and English -- and were first published in the special collection "Mekhanika i tekhnologiya na kompozitsionnite materiali" [Mechanics and Production Methods of Composite Materials] (Sofia, BAN, 1985) and this was handed out to the regular participants in the conference.

During the 3 working days of the conference, a total of 110 reports were given and these were almost evenly distributed in the two sections.

A general view of the participants from abroad and from our nation was that the conference was carried out at a high scientific level and this was expressed both in the discussions as well as in the final session in the statements of the leader of the Soviet delegation, Prof N. V. Churayev, and of Academician J. Nemec and Prof R. Bares. By the reports given and the lively discussion, new contacts were established between the specialists, experience was exchanged and new ideas arose in the study and application of composite materials. General conclusions were drawn to explain the properties of composite materials, for controlling structure formation, for investigating the processes of destruction, for employing new, modern methods of experimental research. The development of these trends in the research being carried out in our country will lead to the obtaining of new composite materials and, respectively, to the saving of labor, materials and energy.

New Technology

Sofia SPISANIE NA BULGARSKATA AKADEMIYA NA NAUKITE in Bulgarian No 1, 1986 pp 79-81

[Unattributed descriptions published under the rubric: "Proposals for Introduction and Introduced New Devices. Materials and Production Methods"]

[Text] The BK 13XX Family of 16-Digit Microcomputer Systems

The Scientific Research Laboratory for Instrument Building and Automation of Biological Experiments (NILUABE) Under the BAN has developed a family of 16-digit microcomputer systems, the BK 13XX. They are protected by a certificate of invention [patent] reg. No 61147 as of 30 May 1983 and reg. No 67037 as of 4 October 1984. The author collective consists of: Senior Science Associate G. Dimitrov (leader), Science Associate P. Mitev, Science Associate N. Baev, Science Associate V. Maslenkov, Science Associate Kh. Badarov, Science Associate L. Stoychev, Science Associate P. Neychev and Science Associate Z. Latev.

The BK 1300 and BK 1302 systems have been introduced at the Scientific-Production Enterprise for Scientific Instrument Building Under the BAN. The technical specifications for these systems have also been worked out at the same enterprise.

The BK 13XX microcomputer systems are program compatible with the following microcomputers MINC 11, POP 11/03, MERA 60 and the minicomputers SM 3, SM 4, DPD11. They can operate under the control of different operational systems. One of them (BIKOS) has been worked out by a collective from the Unified Center for Mathematics and Mechanics Under the BAN with the leader, Prof P. Burnev.

The microcomputer systems have been built completely with devices and elements produced in the socialist countries. These consist of: the Elektronika 60M processor, a 64-k on-line memory, the SM 1604 video terminal, the ES 5074 floppy disc devices, IZOT 0203M1 printer, the SM 5300.01 minitape device, the SM 5400 minidisc device and modules for connecting with the object (ATsP [analog-to-digital convertor], TsAP [digital-to-analog convertor] and programmable timer). The systems make it possible also to connect the DZM 180 and EPSSON printers, the Mikronika 297 plotter, a graphic video terminal, a puncher and a punch card reader.

In terms of their qualities, the BK 13XX minicomputer systems correspond to the embargoed MINC 11.

The systems are designed to solve scientific and technical problems, the automating of scientific research, the automating of administrative and managerial activities, the automating of warehouse systems and so forth. On the basis of the BK 13XX systems, together with the Physiology Institute Under the BAN, microcomputer systems are being developed for automating pharmacological and toxicological research and for automating the research on the contractive and bioelectrical activities of the smooth muscles.

The NIIUABE and the Scientific Production Enterprise for Scientific Instrument Building have developed models of the BK 1300 and BK 1302 systems for over 3 million leva for the needs of the nation and for satisfying the interest shown in the systems abroad. In 1983, exports were over 200,000 foreign exchange leva and in 1984, over 350,000 foreign exchange leva. There are also new orders from abroad.

The NIIUABE and the Scientific Production Enterprise for Scientific Instrument Building under contract orders by the interested organizations will produce both the base configurations of the BK 13XX microcomputer systems as well as the systems developed on their basis for the automating of biological research.

The ABR-02 M Laboratory Fermentor With a Microprocessor Control System

A laboratory fermentor has been developed by the Scientific Research Laboratory for Instrument Building and Automation of Biological Experiments (NIIUABE) Under the BAN and is protected by three inventions (reg. No 57319 of 7 July 1982, reg. No 61411 of 27 July 1983 and reg. No 66336 of 20 July 1984). The leader of the author collective of the inventions and the development of the equipment was Docent St. Tsonkov.

The newly developed device consists of three parts: the biotechnological part, the metering and control part and the power block. The biotechnological

part includes a thermally sterilizable glass vessel (3 and 51), an air filter, a cooler, three peristaltic pumps for supplying the acid, the base and a foam suppressor. The vessel is equipped with a turbine-type agitator driven by a DC electric motor. The speed of the agitator can be adjusted within a range of 0-1,100 rpm.

The metering and controlling part consists of a microprocessor control system and sensors for temperature, dissolved oxygen, pH, the foam formation level, agitator speed and air consumption. Also planned is the possibility of incorporating a supplementary data channel.

For ensuring reliability and compactness, the control part has been developed as a single-bored microcomputer and this has been built on the basis of the SM 601 Bulgarian microprocessor with an on-line memory of 2 kbits and a permanent storage of 16 kbits and has 8 analog inputs and 9 optoinsulated discrete outputs.

The system's software includes a monitor program for processing the data of the measurements, a program for realizing the selected control algorithms (temperature, pH, percentage content of dissolved oxygen, agitator speed and foam formation level) as well as a program for realizing a dialogue input language.

The advantages of the development consist in the fact that its technical and economic indicators are better than foreign models and production is cheaper.

The ABR-02 M laboratory fermentor is designed for laboratory research with microbial cultures. It is usable in microbiology, molecular biology, bacteriology, biochemistry, the food industry and so forth. The device has been put into small-series production at the NIIUABE Under the BAN and is being manufactured under contractual orders for interested organizations in Bulgaria and abroad. In 1984, over 100,000 foreign exchange leva of exports were sold to the Soviet-bloc countries. To the economic effect from introducing the new device, we must add the savings in foreign exchange for the non-Soviet countries.

A Fiber-Optical System for Transmitting Digital Data and the Support and Operating Equipment

The Electronics Institute (IE) Under the BAN has developed our nation's first fiber-optical system designed for supervision and control in automating production processes in industry as well as the corresponding monitoring and metering equipment for its maintenance and operation. The author collective includes: Senior Science Associate M. Drazhev (leader), Science Associate L. Khristov and Science Associate B. Stoykov.

The fiber-optical system has a closed structure (a Pierce circle), in providing the data volume in a digital form with the Manchester code between four receiving-transmitting points with microprocessor control. Each point can interrupt the information circle and transmit data, but if there is no such permission, it transmits the information received and circulating in the circuit.

The sensitivity of the optic receivers is -50 decibel meter for BER-10^{-9} with a speed of data exchange up to 2 Mbits/second. The optical pulse power introduced from the transmitters into the standard gradient light conduit of 50/125 micrometers is +3 decibel micron. The maximum distance between the receiving-transmitting points with an attenuation of the optical cables to 5 decibel/km, is around several kilometers.

The system has increased noise resistance due to the use of an original circuitry design worked out at the IE and protected by the certificate of invention reg. No 65214 "A Digital Receiver for a Fiber-Optical System" as of 24 April 1984.

The maintenance and operational control equipment include a standard oscillator for optical pulses with a repetition frequency of 500 kilohertz, a pulse ratio of 0.5 and a power introduced into the light conduit of +3 decibel micron, as well as a master receiver for measuring the power of the optical pulses in a range from -60 decibel micron to -20 decibel micron directly in decibels. The operating wave length is around 0.85 micrometers.

The system is built completely from optoelectronic elements, optical cables and optical couplings produced in Bulgaria.

The system developed at the IE and the equipment for its maintenance and operational control are to be introduced by active participation of the IE Under the BAN and the Central Scientific Research Institute for Full Automation (TsNIKA) Under the Ministry of Machine Building. Experiments with the system have been conducted at the Plant for Metalcutting Machines in Silestra. A significant economic effect which can be obtained in introducing such a system from the TsNIKA into industry is brought about by the automating of production processes as well as by the end of importing from the capitalist world.

10272
CSO: 2202/18

END